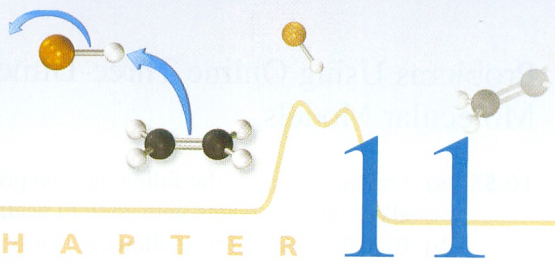
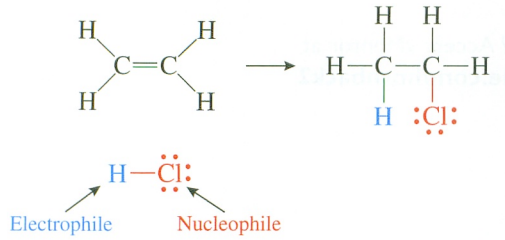
Additions to Carbon–Carbon Double and Triple Bonds



REACTIONS OF ALKENES AND ALKYNES

CHAPTER 11

THE REACTION that is presented in this chapter results in the addition of two groups—an electrophile and a nucleophile—to the carbons of a carbon–carbon double or triple bond. In the following example of this addition reaction, a proton (the electrophile) and a chloride ion (the nucleophile) add to the carbons of ethene to produce chloroethane:



The features of this reaction that will be examined include the following:

- The mechanism of the reaction
- The effect of substituents on the double bond on the rate of the reaction
- The regiochemistry of the reaction
- The stereochemistry of the reaction
- The various combinations of electrophiles and nucleophiles that undergo this reaction
- The variations in mechanism, regiochemistry, and stereochemistry that occur with these different reagents
- Similar reactions that occur with carbon–carbon triple bonds

A large number of reactions are presented in this chapter. As was the case with the previous reactions we have

MASTERING ORGANIC CHEMISTRY

- Predicting the Products, Including Regiochemistry and Stereochemistry, Resulting from Addition Reactions of Alkenes
- Predicting the Products, Including Regiochemistry and Stereochemistry, Resulting from Addition Reactions of Alkynes
- Understanding the Mechanisms of These Addition Reactions
- Recognizing When Rearranged Products Are Likely to Occur
- Predicting How the Rate of Addition Varies with the Structure of the Alkene
- Predicting the Products of Additions to Conjugated Dienes
- Using Addition Reactions to Synthesize Other Compounds

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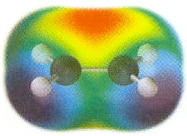
seen, identifying the electrophile and the nucleophile will make the task of remembering all of these reactions much easier. Keep the general mechanism in mind and note what changes are caused in the mechanism by the different reagents as each is discussed.

11.1 The General Mechanism

The simplest version of the mechanism for this addition reaction occurs in two steps. First, the electrophile adds to the double bond, producing a carbocation intermediate. In the second step the nucleophile adds to the carbocation. This step is identical to the second step of the S_N1 reaction. Because the initial species that reacts with the double bond is an electrophile, the reaction is called an **electrophilic addition reaction.**



Electrostatic potential map of the alkene nucleophile

In the first step the nucleophile is the alkene, or, more specifically, the highest-energy pair of electrons of the alkene: the pi electrons of the double bond. Because these electrons, are in a bonding MO rather than in a higher-energy nonbonding MO, they are only weakly nucleophilic, so a relatively strong electrophile, such as H^+ from a strong acid, is needed to react with them. Most of these addition reactions are run under acidic or neutral conditions to avoid destroying the electrophiles, which are all fairly strong Lewis acids.

The product of the first step is a high-energy carbocation intermediate. Forming this reactive intermediate is the slow step of the mechanism. As was the case in the S_N1 reaction, the transition state for this step resembles the carbocation (recall the Hammond postulate; see Section 8.6). Therefore, structural features that stabilize the carbocation also stabilize the transition state leading to it, thus lowering the activation barrier and resulting in a faster rate of reaction. We know from Chapter 8 the various features that stabilize carbocations. The presence of electron-donating alkyl groups on the positive carbon stabilizes the carbocation; tertiary carbocations are more stable than secondary carbocations, and secondary carbocations are more stable than primary carbocations. Therefore, alkyl substituents on the double bond accelerate the reaction. Resonance stabilization of the carbocation also speeds up the reaction. The presence of groups that withdraw electrons destabilizes the carbocation and

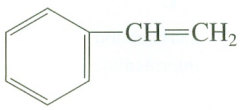
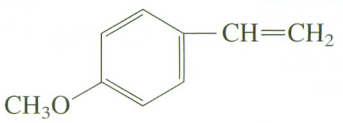
results in a slower reaction rate. We also know that carbocations are prone to rearrange if a more stable cation can result. Rearrangements do occur in these electrophilic addition reactions, so we must always examine the carbocation to see whether rearrangement is likely.

Because the second step is the same as the second step in the S_N1 mechanism, similar nucleophiles, such as H_2O and the halide ions, are found here. In addition, there are electrophiles and nucleophiles that we have not yet encountered that undergo this reaction. Some of these cause variations on the mechanism presented earlier. However, the general theme of the electrophile adding first and ultimate formation of a product with the electrophile bonded to one carbon of the initial double bond and the nucleophile bonded to the other remains unchanged. Let's look at the various combinations of electrophiles and nucleophiles that are commonly employed and see how the details of the reaction are affected in each case.

PROBLEM 11.1

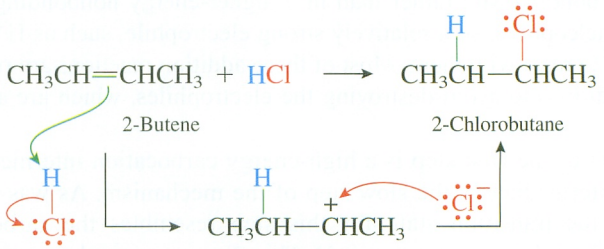
Arrange these alkenes in order of increasing rate of reaction with HCl:

a) $CH_3CH_2CH{=}CH_2$ $\quad$ $CH_2{=}CH_2$ $\quad$ $CH_3CH_2\overset{\displaystyle CH_3}{\overset{|}{C}}{=}CH_2$

b)  $\quad$ $CH_3CH{=}CH_2$ $\quad$ 

11.2 Addition of Hydrogen Halides

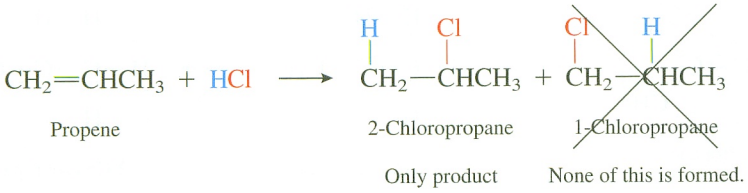
All of the halogen acids, HF, HCl, HBr, and HI, add to alkenes to give alkyl halides, as shown in the following example in which hydrogen chloride adds to 2-butene:



In this example the electrophile is a proton and the nucleophile is a chloride anion. The mechanism is just as described in the previous section; first the electrophilic proton adds to produce a carbocation intermediate, and then the chloride nucleophile bonds to the carbocation.

Because 2-butene is a symmetrical alkene, it does not matter which carbon initially bonds to the proton. Only one product, 2-chlorobutane, is possible. In the case of an unsymmetrical alkene—that is, one with different substituents on the two carbons of the double bond—two products could be formed, depending on which carbon bonds to the

electrophile and which bonds to the nucleophile. For example, the reaction of hydrogen chloride with propene could produce 1-chloropropane or 2-chloropropane:



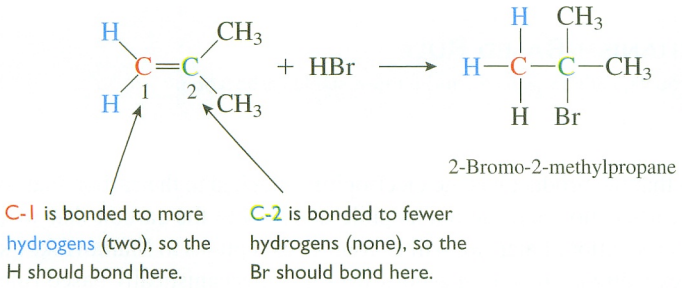
When this reaction is run in the laboratory, the only product formed is 2-chloropropane. No 1-chloropropane is observed. A reaction such as this one that produces only one of two possible orientations of addition is termed a **regiospecific reaction.** (A reaction that produces predominantly one possible orientation but does form some of the product with the other orientation is termed a **regioselective reaction.**)

In 1869 Vladimir Markovnikov studied the regiochemistry of a large number of these addition reactions. On the basis of his observations, he postulated an empirical rule that can be used to predict the orientation of additions to alkenes:

MARKOVNIKOV'S RULE

In addition reactions of HX to alkenes, the H bonds to the carbon with more hydrogens (fewer alkyl substituents) and the X bonds to the carbon with fewer hydrogens (more alkyl substituents).

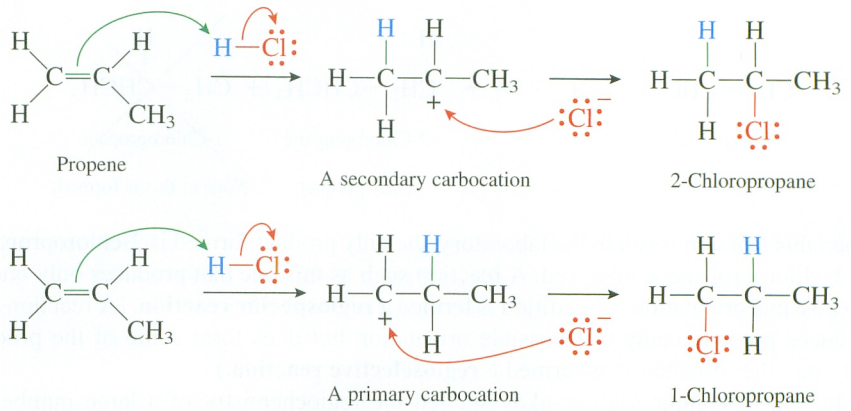
As an example, Markovnikov's rule predicts that the addition of hydrogen bromide to 2-methylpropene should produce 2-bromo-2-methylpropane:



When the reaction is run in the laboratory, only the product predicted by Markovnikov's rule is observed.

Markovnikov's rule was empirical; that is, it was based on observation only. At the time it was proposed, the concept of organic reaction mechanisms had not yet been imagined; so it was impossible to provide a theoretical basis for why the H added to one carbon and the X to the other. Now that we know the mechanism for the reaction, it is easy to understand why these reactions are regiospecific. In fact, if we write the mechanism for the additions to give both possible products, we can predict the preferred product simply on the basis of what we already know about carbocations. It is much better to make predictions based on the mechanism of the reaction because cases that are exceptions to the empirical rule will be readily apparent.

The mechanisms for the two possible orientations of addition of HCl to propene are as follows:



The first mechanism, which leads to the Markovnikov product 2-chloropropane, proceeds via a secondary carbocation. The second mechanism, which would lead to the unobserved product 1-chloropropane, proceeds via a primary carbocation. Because a secondary carbocation is lower in energy than a primary carbocation, the first mechanism should be preferred over the second mechanism. In fact, formation of the secondary carbocation is enough faster than formation of the primary carbocation that the first mechanism occurs to the exclusion of the second.

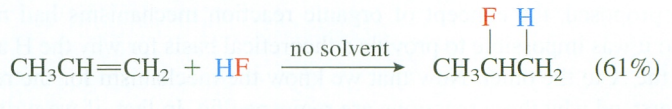
We can now see the reason behind Markovnikov's rule. If the proton adds to the carbon with more hydrogens, the positive carbon, where the nucleophile will ultimately bond, is bonded to more alkyl groups, resulting in a more stable carbocation. A more modern version of Markovnikov's rule, based on this mechanistic reasoning is as follows:

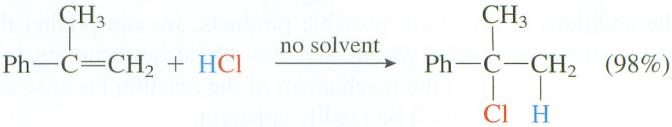
▶ MECHANISM-BASED RULE

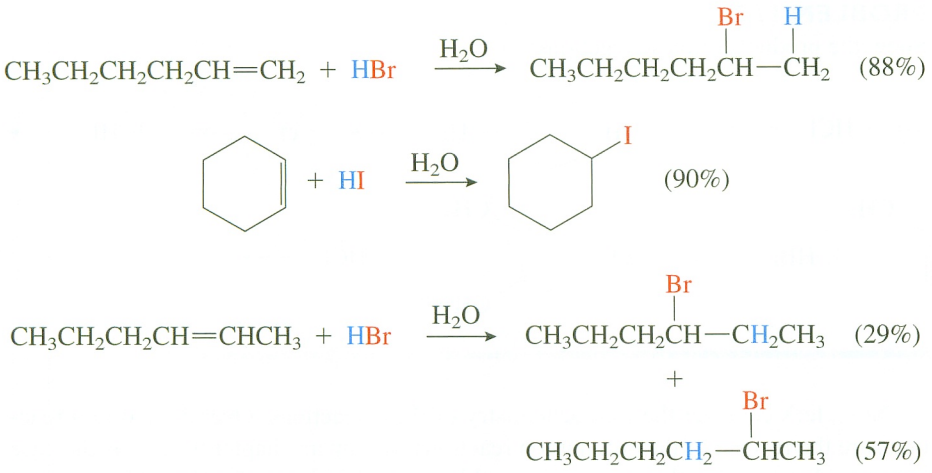
The electrophile adds so as to form the more stable carbocation.

This means that the product has the electrophile attached to the carbon that would be less stable as a carbocation and the nucleophile attached to the carbon that would be more stable as a carbocation. Later, we will encounter exceptions to Markovnikov's rule. However, these exceptions are still in accord with this mechanistically based rule.

Some examples of additions of hydrogen halides are provided by the following equations. As you look at each example, try to predict the regiochemistry of the product before looking at the actual product that is formed.





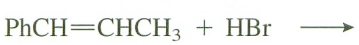


PROBLEM 11.2

Show the structures of the carbocations that are formed in the reaction of HBr with 2-hexene and explain why two products are formed.

PRACTICE PROBLEM 11.1

Show the product of this reaction:

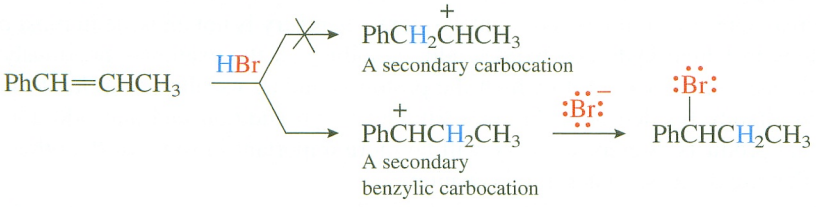


Strategy

Identify the electrophile and the nucleophile. In this problem the electrophile is H^+ and the nucleophile is bromide anion. Add the H^+ to one carbon so that the more stable carbocation is formed at the other carbon. Add the bromide nucleophile to the other carbon.

Solution

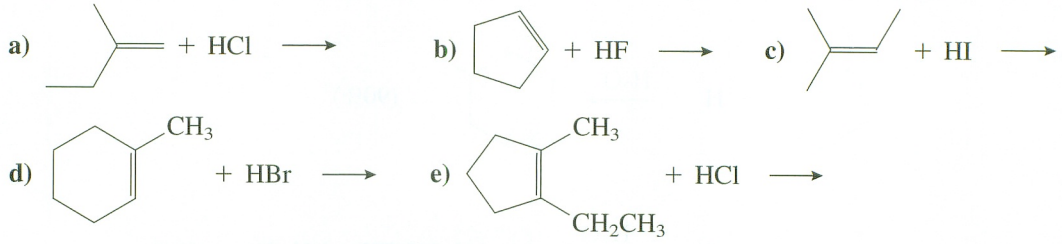
The two possible carbocations that can be formed by the addition of H^+ are shown in the following equations:



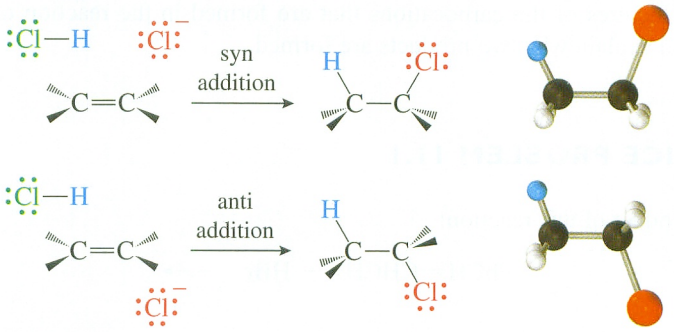
Because of its resonance stabilization, the secondary benzylic carbocation is more stable than the secondary carbocation, so the product has the bromine (nucleophile) bonded to the carbon attached to the phenyl group.

PROBLEM 11.3

Show the products of these reactions:



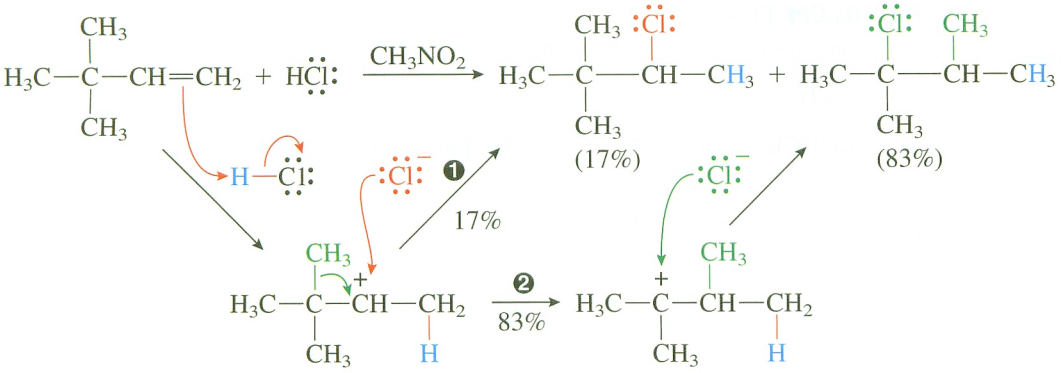
Next, let's consider the stereochemistry of these reactions. Overall, addition reactions are the reverse of the elimination reactions we saw in Chapter 9. As was the case with the eliminations, there are two possible stereochemistries for the addition—syn and anti:



In a syn addition the electrophile and the nucleophile both add from the same side of the plane of the double bond; in an anti addition they add from opposite sides of this plane.

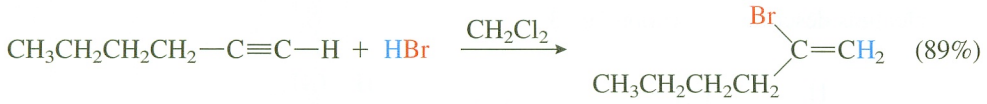
The mechanism for the addition of the hydrogen halides to alkenes proceeds through a carbocation intermediate. As was the case in the S_N1 reaction, the nucleophile can approach the planar carbocation equally well from either side, so we expect that the products should result from a mixture of syn and anti addition. Indeed, this is often the case. Under some conditions, however, the stereochemisty results from predominant syn addition, whereas anti addition is the favored pathway under other conditions. This occurs because these reactions are often conducted in nonpolar solvents in which ion pair formation is favored. The details of how this may affect the stereochemistry of these reactions are complex. Fortunately, stereochemistry is not an issue in most of the reactions in which hydrogen halides add, including all the examples previously presented, because the carbon to which the proton is adding usually has at least one hydrogen already bonded to it. In such situations, syn addition and anti addition give identical products. Stereochemistry will be more important in some of the other reactions that are discussed later in this chapter.

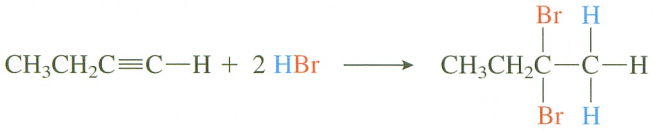
Because carbocations are intermediates in these reactions, rearrangements can occur. The carbocation formed initially in the following example is secondary. Part of the time (17%), the chloride nucleophile intercepts the carbocation before it has a chance to rearrange. But a majority of the time (83%), the carbocation rearranges to a more stable tertiary carbocation, which, on reaction with chloride ion, produces the rearranged product.



❶ This secondary carbocation reacts with chloride (17%)
❷ and rearranges to the more stable tertiary carbocation (83%).

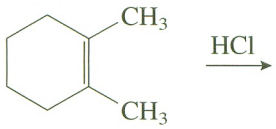
The hydrogen halides also add to the triple bond of alkynes. The regiochemistry of the reactions follows Markovnikov's rule. It is usually possible to add to just one of the pi bonds, producing a vinyl halide, or to both of the pi bonds, producing a dihaloalkane. Some examples are provided in the following equations:





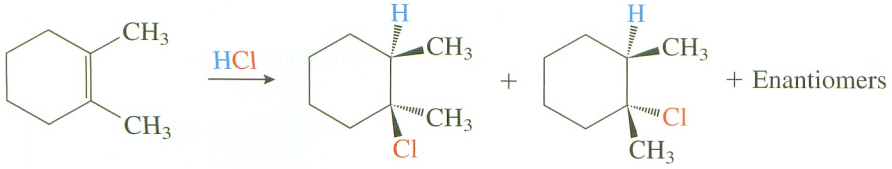
PRACTICE PROBLEM 11.2

Show the products of this reaction:



Solution

Because the addition of HCl to an alkene proceeds through a carbocation intermediate, products from both syn and anti addition are usually formed. This means that products are expected with the H and the Cl both cis and trans.



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PROBLEM 11.4

Show the products of these reactions:

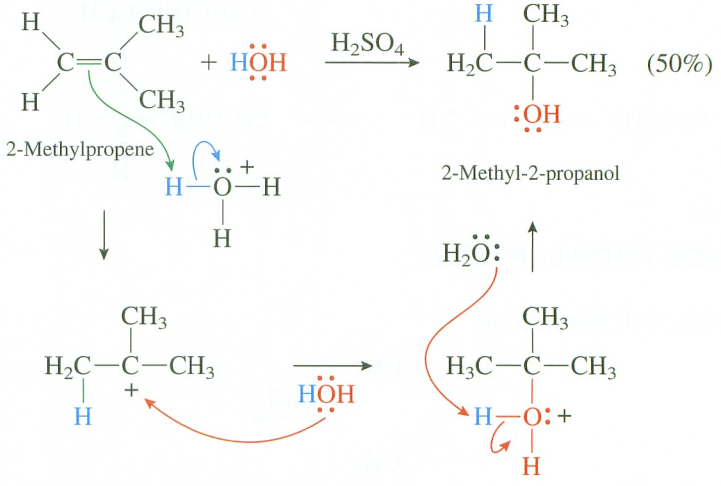
a) $CH_3CHCH{=}CH_2$ (CH$_3$ on the CH) $\xrightarrow{HBr}$

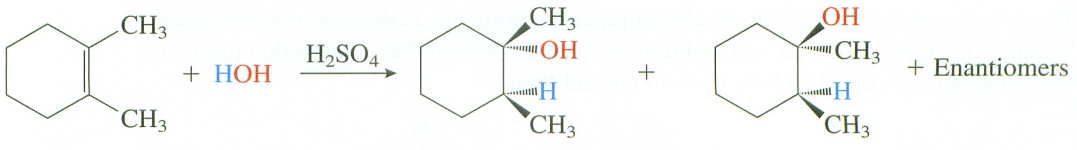
b) $PhC{\equiv}CH \xrightarrow{HBr}$

c)  $\xrightarrow{2\ HBr}$

11.3 Addition of Water (Hydration)

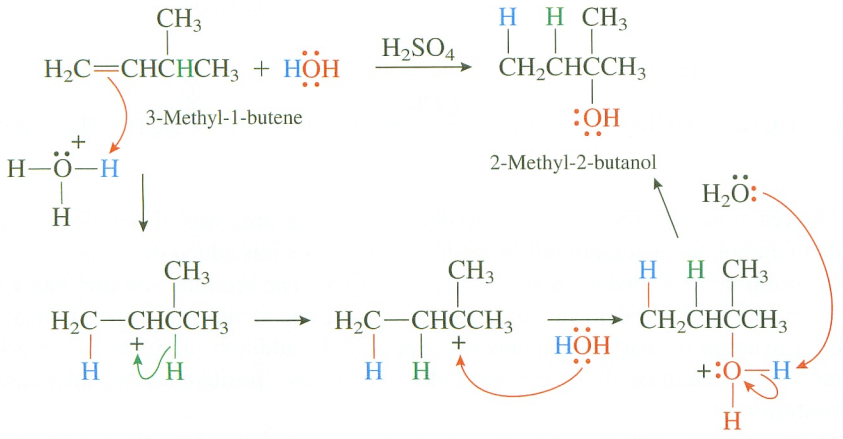
Treatment of an alkene with a strong acid, such as sulfuric acid, that has a relatively nonnucleophilic conjugate base results in the addition of the elements of water (H and OH) to the double bond. This reaction has many similarities to the addition of the halogen acids described in Section 11.2. First H^+ adds to produce a carbocation and then water acts as the nucleophile. The reaction follows Markovnikov's rule and the stereochemistry is that expected for a reaction that involves a carbocation—loss of stereochemistry. Some examples are provided in the following equations. Note that the mechanism is the exact reverse of the E1 mechanism for acid-catalyzed dehydration of alcohols described in Section 10.13.





1,2-Dimethylcyclohexene *cis*-1,2-Dimethylcyclohexanol *trans*-1,2-Dimethylcyclohexanol

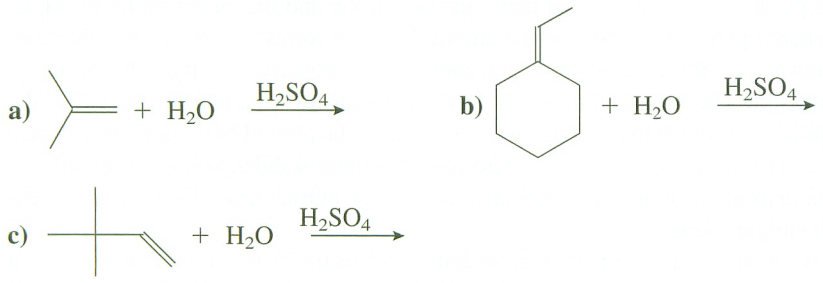
The yields in this reaction are often relatively low because of the strongly acidic conditions. In addition, the reaction conditions are very favorable for carbocation rearrangements as shown in the following example:



For these reasons, acid-catalyzed hydration is often not the method of choice for preparing alcohols from alkenes. Another reaction that accomplishes this same transformation, often in higher yield, is described in Section 11.6.

PROBLEM 11.5

Show the products of these reactions:

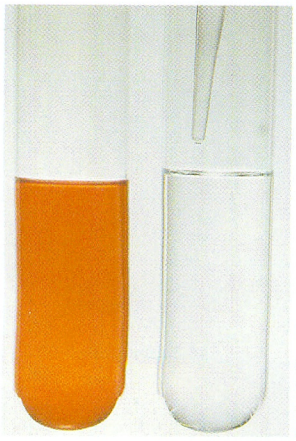


PROBLEM 11.6

Show all of the steps in the mechanism for the addition of water to propene catalyzed by sulfuric acid. Explain whether propene or phenylethene ($PhCH{=}CH_2$) has a faster rate in this reaction.

11.4 Addition of Halogens

Both Cl_2 and Br_2 add to carbon–carbon double bonds to produce dihalides as illustrated in the following examples. The other halogens are not commonly used—F_2 because it is too reactive and I_2 because it is not reactive enough. These reactions are usually run in an inert solvent such as CCl_4, $CHCl_3$, or CH_2Cl_2.



Charles D. Winters

A solution of Br_2 in carbon tetrachloride is red. When a few drops of an alkene are added, the color disappears.

$$CH_3CH{=}CHCH_2CH_3 + Cl_2 \xrightarrow{CHCl_3} CH_3\underset{Cl}{CH}{-}\underset{Cl}{CH}CH_2CH_3 \quad (81\%)$$

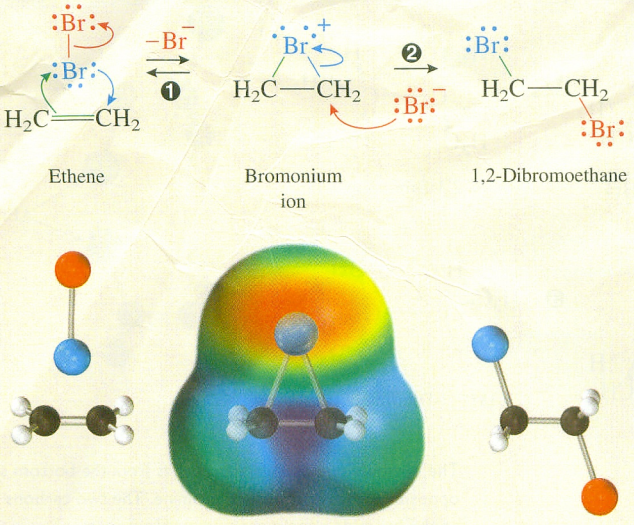
2-Pentene — 2,3-Dichloropentane

$$PhCH{=}CH{-}\overset{O}{\overset{\|}{C}}OCH_2CH_3 + Br_2 \xrightarrow{CCl_4} PhCH(Br){-}CH(Br){-}\overset{O}{\overset{\|}{C}}OCH_2CH_3 \quad (85\%)$$

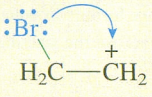
The reaction with bromine is a classical test for the presence of double (or triple) bonds in an unknown compound. In the test, the unknown is added dropwise to a solution of bromine in a solvent such as CCl_4 or CH_2Cl_2. The bromine solution has a red-brown color. If the unknown contains carbon–carbon double or triple bonds, the addition reaction is nearly instantaneous. Because the addition products are colorless, the rapid disappearance of the bromine color constitutes a positive test for the presence of unsaturation.

The mechanism of these additions has an interesting variation from the one for the addition of the hydrogen halides. It begins with electrophilic attack of the halogen at the pi electrons of the double bond, as shown in Figure 11.1. As the bromine–bromine bond breaks in a heterolytic manner, the bromine that is becoming electron deficient acts as the electrophile and adds to the double bond. However, a carbocation is not produced in this addition. Instead, an unshared pair of electrons on the attacking bromine forms a bond to the other carbon. These three events happen simultaneously: the bromine–bromine bond breaks, the pi electrons form a bond between one carbon and the electrophilic bromine, and an unshared pair of electrons on the adding bromine forms a bond to the other carbon. The result is a three-membered ring containing a positively charged bromine—a **bromonium ion.** The bromonium ion is formed instead of a carbocation because the bromonium ion is more stable. It has an octet of electrons around both carbons and also the bromine. Having the octet rule satisfied provides more stabilization even though the positive charge is on the more electronegative bromine. Chlorine reacts by a similar mechanism with simple alkenes.

When we first encounter a new intermediate, such as the bromonium ion, we should compare it to other similar species that we have learned about to predict how it is likely to behave. What other three-membered rings containing a positively charged heteroatom have we seen? The answer is the protonated epoxide that was discussed in Section 10.10. The chemistry of the bromonium ion is very similar to that of the protonated epoxide. It reacts with nucleophiles—bromide ion, in this case—resulting in opening of the ring. As was the case with the protonated epoxide, this nucleophilic attack has characteristics of both the S_N2 and S_N1 reactions. The stereochemistry is that of an S_N2 reaction: the nucleophilic bromide approaches from the side opposite the leaving bromine. This results in an overall anti addition of the two bromines. The regiochemistry is that of an S_N1 reaction: the nucleophile bonds to the carbon that would be more stable as a carbocation because there is more positive charge located there. Of course, we cannot tell which bromine came in as the electrophile and which came in as the nucleophile in these reactions. However, we will encounter similar reactions later in which the electrophile and the nucleophile can be distinguished.



❶ The electrophile is the bromine molecule. One Br leaves as a negative ion. As this Br leaves, the other Br becomes electrophilic and attracts the electrons of the alkene pi bond. If a carbocation were formed at this stage, it would look like this.



However, in this carbocation, the Br is very close to the positive carbon and can easily use a pair of its unshared electrons to form a bond to the carbon. The resulting species, a bromonium ion, is more stable than the carbocation because the octet rule is satisfied for all of the atoms. The carbocation is not actually formed in the reaction. Instead, the bromonium ion is formed directly. As the bromine–bromine bond is breaking, both carbon–bromine bonds are forming simultaneously.

❷ The bromonium ion resembles a protonated epoxide (see Section 10.10) in both structure and reactions. Therefore, when the nucleophilic bromide attacks to open the three-membered ring, it approaches from the side opposite the other bromine. The result is an anti addition of the two bromines to the double bond.

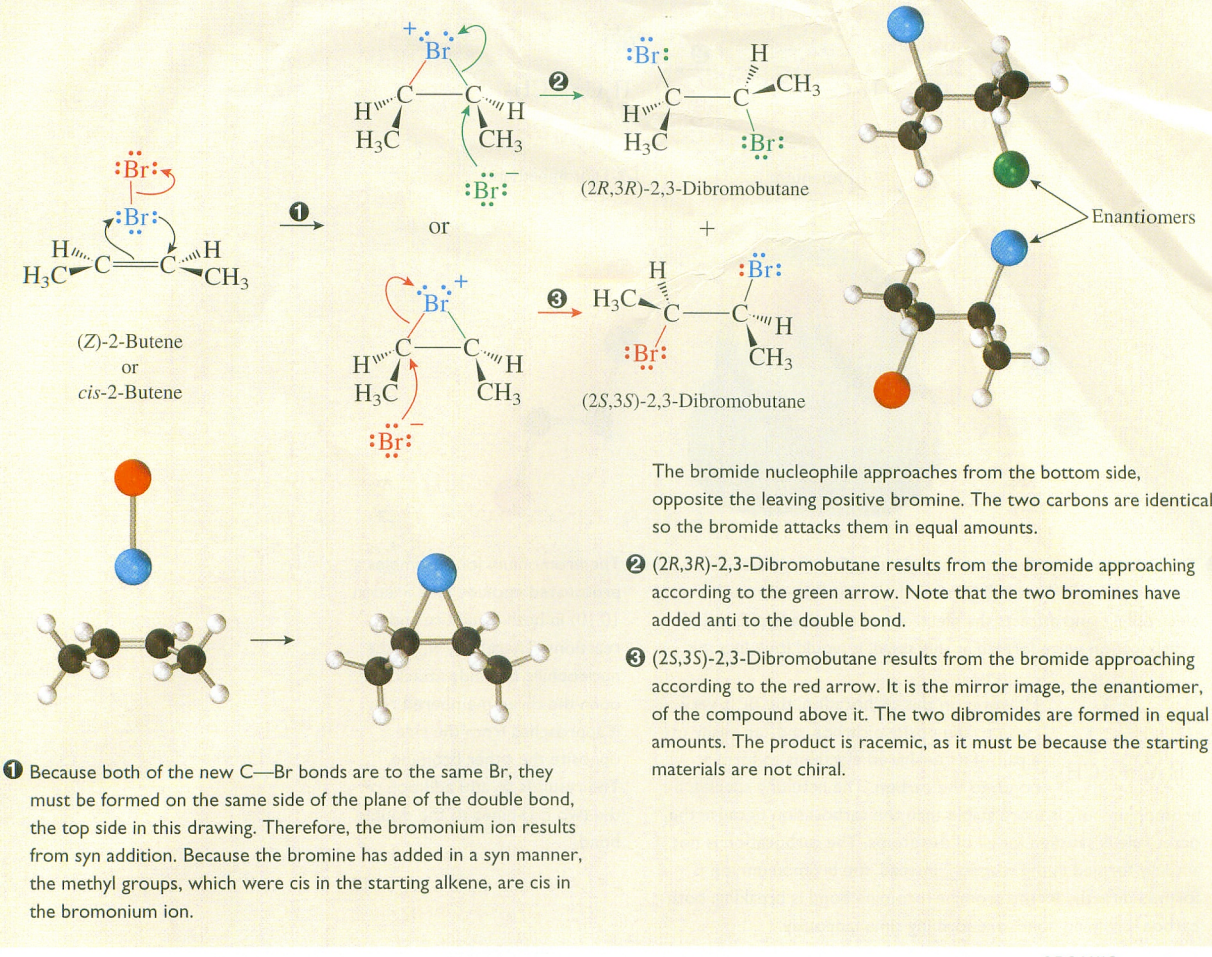
Figure 11.1

MECHANISM OF THE ADDITION OF BROMINE TO ETHENE.

Let's examine the stereochemistry of the reaction of bromine with 2-butene:

2-Butene — 2,3-Dibromobutane

Considering stereochemistry, there are two stereoisomers of the starting alkene (cis and trans) and three stereoisomers of the product dibromide (the *d*-, *l*-, and *meso*-isomers). The reaction of bromine with (*Z*)-2-butene is shown in Figure 11.2, and the reaction of

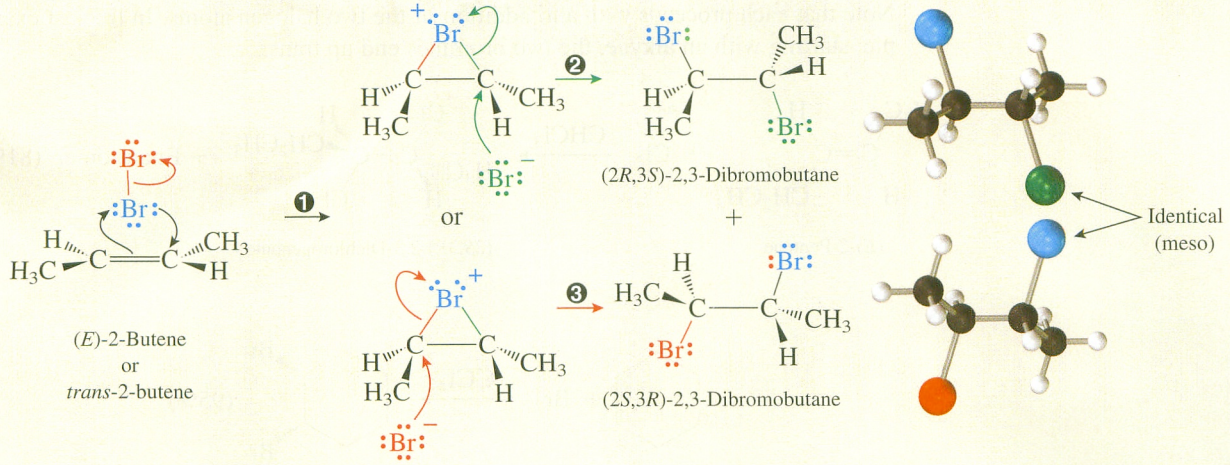


Active Figure 11.2 ORGANIC Chemistry Now™

MECHANISM OF THE ADDITION OF BROMINE TO (Z)-2-BUTENE (*CIS*-2-BUTENE). Test yourself on the concepts in this figure at **OrganicChemistryNow.**

bromine with (*E*)-2-butene is shown in Figure 11.3. As can be seen from these figures, anti addition to (*Z*)-2-butene produces only (*d,l*)-2,3-dibromobutane as a racemic mixture. (Remember, if the reactants are not chiral, the products, if chiral, must be produced as a racemic mixture.) Anti addition to (*E*)-2-butene produces only the *meso*-diastereomer. The reactions are **stereospecific;** that is, one diastereomer of the reactant produces only one diastereomer of the product.

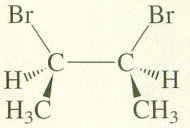
As expected for an electrophilic addition, the reaction rate increases as alkyl groups are substituted on the double bond. The electron-donating alkyl groups make the alkene more nucleophilic. Table 11.1 lists the relative rates of bromination of a series of alkenes. As can be seen from this table, replacing all four of the hydrogens of ethene with methyl groups results in an increase in the rate of the reaction by a factor of 2 million.



❶ The bromine has added in a syn manner, the methyl groups, which were trans in the starting alkene, are trans in the bromonium ion. The bromide nucleophile then approaches from the bottom side, opposite the leaving positive bromine. The two carbons are identical so the bromide attacks them in equal amounts.

❷ (2*R*,3*S*)-2,3-Dibromobutane results from the bromide approaching according to the green arrow. Note that the two bromines have added anti to the double bond.

❸ (2*S*,3*R*)-2,3-Dibromobutane results from the bromide approaching according to the red arrow. It is a superimposable mirror image of the compound above it. The two dibromides are identical—the product is *meso*-2,3-dibromobutane. If the compound is shown in its most symmetrical conformation, the internal plane of symmetry is apparent.

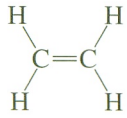
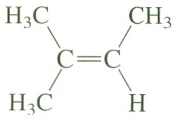
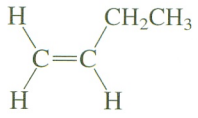
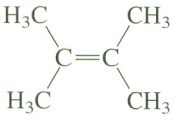
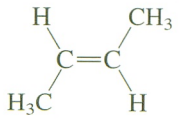


Active Figure 11.3

ORGANIC Chemistry Now™

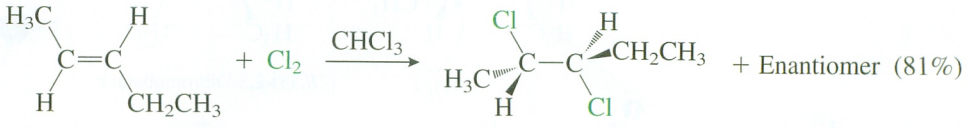
MECHANISM OF THE ADDITION OF BROMINE TO (*E*)-2-BUTENE (*TRANS*-2-BUTENE). Test yourself on the concepts in this figure at **OrganicChemistryNow.**

Table 11.1 Relative Rates of Reaction of Alkenes with Bromine

Alkene	Relative Rate	Alkene	Relative Rate
	1		1×10^5
	1×10^2		2×10^6
	2×10^3		

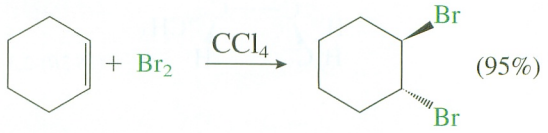
The reaction is the alkene plus Br_2 in methanol as solvent.

Some examples of these addition reactions are provided in the following equations. Note that each proceeds with anti addition of the two halogen atoms. In the last example, starting with an alkyne, the two bromines end up trans.



(*E*)-2-Pentene

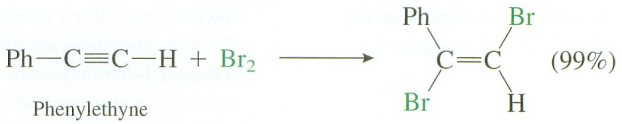
(2*S*,3*R*)-2,3-Dichloropentane



Cyclohexene

trans-1,2-Dibromocyclohexane

Racemic

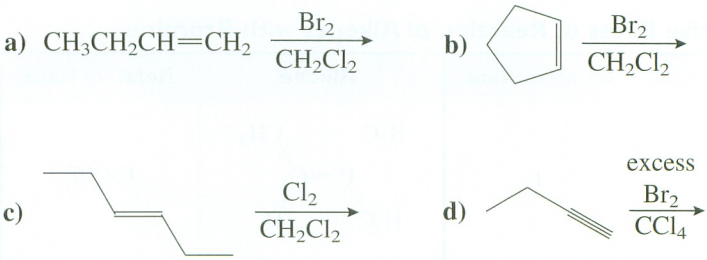


Phenylethyne

(*E*)-1,2-Dibromo-1-phenylethene

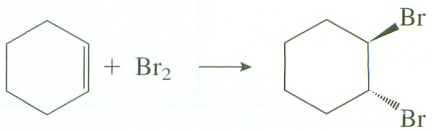
PROBLEM 11.7

Show the products of these reactions:



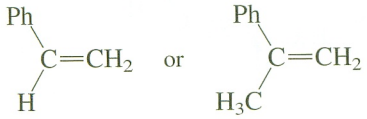
PROBLEM 11.8

Show all of the steps, including stereochemistry, in the mechanism for this reaction:



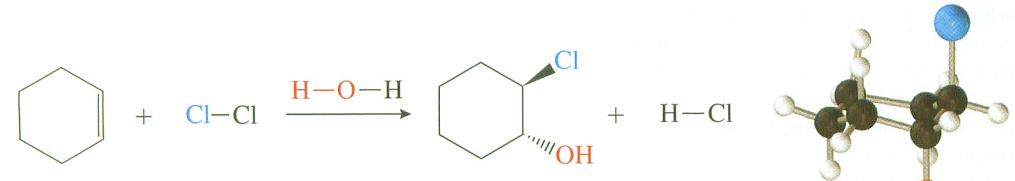
PROBLEM 11.9

Explain which of these compounds has the faster rate of reaction with Br_2:



11.5 HALOHYDRIN FORMATION

The reactions of chlorine and bromine with alkenes described in the previous section are conducted in inert solvents such as CCl_4 and CH_2Cl_2. In these reactions the only nucleophile that is present to react with the halonium ion is the halide anion. However, if the reaction is performed in a nucleophilic solvent, such as water, then a water molecule can act as the nucleophile, resulting in the addition of a halogen and a hydroxy group to the double bond.



Cyclohexene

trans-2-Chlorocyclohexanol
+ Enantiomer
(a halohydrin)

The product is called a halohydrin. Because the concentration of the water molecules is so much higher than the concentration of the halide anions (water is the solvent), water wins the competition to act as the nucleophile, and only the halohydrin is formed in significant amounts.

The mechanism for this reaction is very similar to that for the addition of halogens as described in Section 11.4. First the chloronium ion is formed in exactly the same manner as before. Water then acts as a nucleophile, approaching the carbon from the side opposite the chlorine that it is displacing. This results in an anti addition of the chlorine and hydroxy group. As was the case for both the opening of the halonium ion ring (Section 11.4) and the opening of a protonated epoxide ring (Section 10.10), this opening of the halonium ion ring by water has characteristics of both an S_N1 and an S_N2 reaction. It proceeds with S_N2 stereochemistry (inversion) and S_N1 regiochemistry (the nucleophile attaches to the carbon that is more stable as a carbocation). The electrophile and the nucleophile are different here, so it is possible to see to which carbon each has added. The mechanism for this reaction is given in Figure 11.4 for an example in which both stereochemistry and regiochemistry of the reaction can be observed in the product.

One of the major uses of these halohydrins is for the preparation of epoxides. Treatment of the halohydrin with base, such as NaOH or KOH, results in deprotonation of the alcohol followed by an intramolecular nucleophilic substitution (see Section 10.3), as shown in the following example. Remember that the nucleophilic oxygen must displace the chlorine from the opposite side, resulting in inversion of configuration at that carbon.

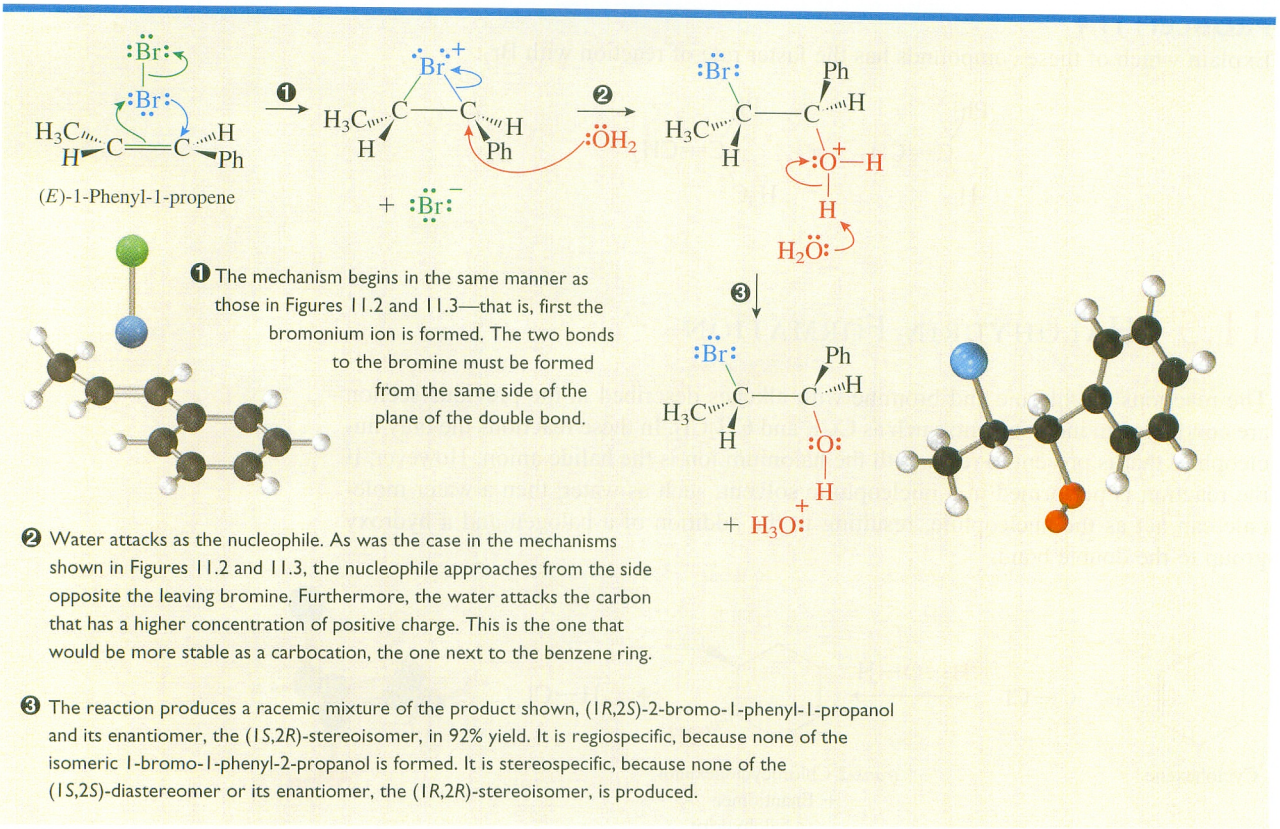
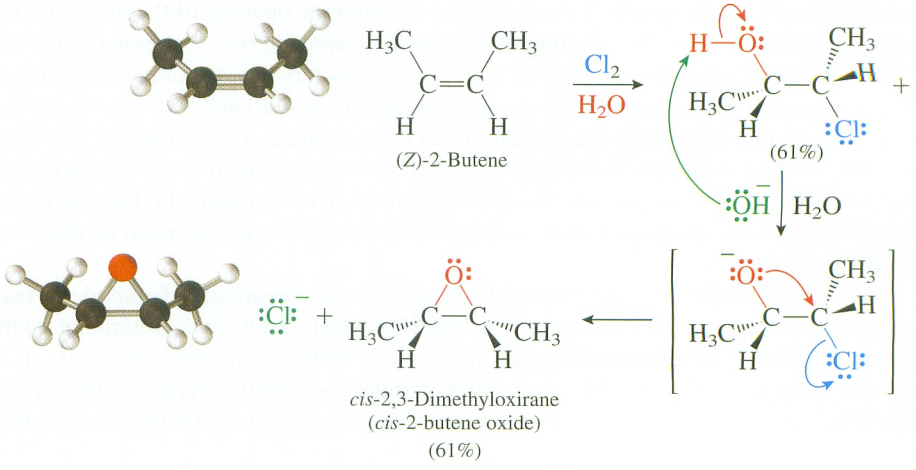


Figure 11.4

MECHANISM OF THE ADDITION OF BROMINE TO AN ALKENE IN WATER.



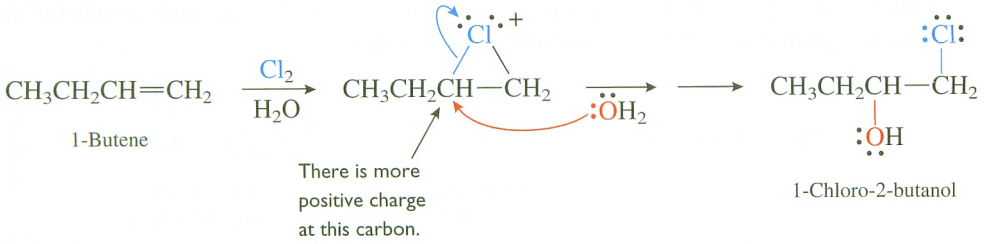
PRACTICE PROBLEM 11.3

Show the product of this reaction:

$$CH_3CH_2CH{=}CH_2 \xrightarrow[H_2O]{Cl_2}$$

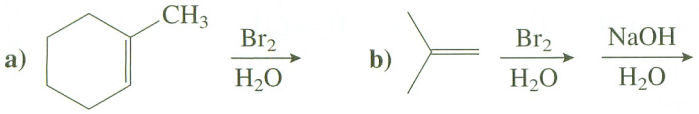
Solution

First a chloronium ion is formed. Then water acts as a nucleophile and attacks at the carbon of the chloronium ion that has more positive charge. In this case it is the secondary carbon rather than the primary carbon that is attacked by water:



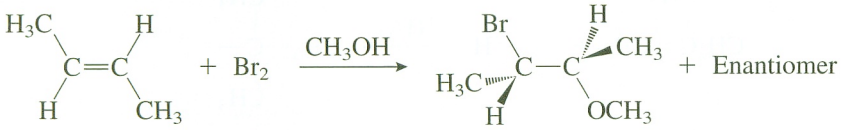
PROBLEM 11.10

Show the products of these reactions.



PROBLEM 11.11

The reaction of an alkene with bromine in an alcohol as solvent produces an ether as the product. Show a mechanism for the following reaction and explain the stereochemistry of the product:



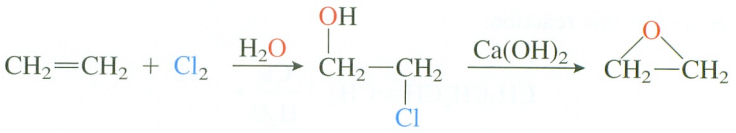
Focus On

Industrial Addition Reactions

Several addition reactions have been or are currently used on a large scale in industrial chemical plants. For example, an older method for the preparation of ethylene oxide employed the addition of chlorine to ethylene in water to form ethylene chlorohydrin or 2-chloroethanol. (In industry, ethene is almost always called ethylene.) Treatment of the chlorohydrin with calcium hydroxide results in the formation of ethylene oxide, which is an important intermediate in the manufacture of ethylene glycol and other products (see the Focus On box on page 375). However, this method is wasteful of

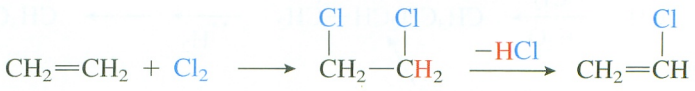
Continued

chlorine (Cl_2 is added, but there is no chlorine in the final product), so it has been replaced with a more efficient process.



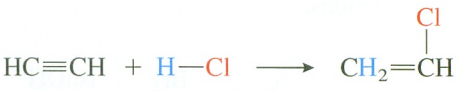
2-Chloroethanol (ethylene chlorohydrin) — Oxirane (ethylene oxide)

More than 18 billion pounds of ethylene dichloride (1,2-dichloroethane) are currently manufactured each year by the addition of chlorine to ethylene. Elimination of HCl from ethylene dichloride produces vinyl chloride, which is the starting material for the production of poly(vinyl chloride), an important polymer:



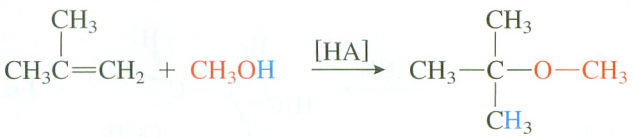
1,2-Dichloroethane (ethylene dichloride) — Chloroethene (vinyl chloride)

An obsolete method for the production of vinyl chloride employed the addition of HCl to acetylene:



Ethyne (acetylene)

One of the fastest-growing petrochemicals of recent times was methyl *tert*-butyl ether (MTBE). More than 13 billion pounds per year of this chemical were manufactured by the acid-catalyzed addition of methanol to isobutylene:



2-Methylpropene (isobutylene) — MTBE

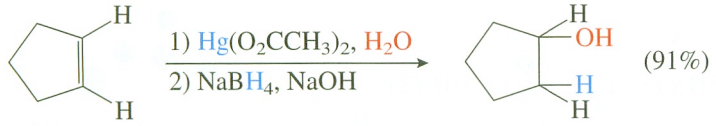
MTBE was initially added to unleaded gasoline to increase its octane rating when leaded gasoline was being phased out. Later it was added for environmental reasons. Gasoline that contains a small percentage of oxygen in its molecules burns cleaner and produces less carbon monoxide than gasoline without oxygen. Therefore, certain large urban areas that suffer from carbon monoxide pollution require the addition of oxygenated compounds, either ethanol or MTBE, to gasoline during the winter months when this pollution is at its worst. Recently, however, MTBE has been found in drinking water supplies due to leakage from gasoline storage tanks. Because MTBE makes water smell and taste foul, even at very low concentrations—in addition to having health concerns—its use is being phased out.

PROBLEM 11.12

Show all of the steps in the mechanism for the formation of MTBE from methanol and isobutylene.

11.6 Oxymercuration–Reduction

In addition to the hydration reaction described in Section 11.3, the oxymercuration–reduction reaction can be used to add the elements of water to a carbon–carbon double bond in a two-step process. First the alkene is reacted with mercuric acetate, $Hg(O_2CCH_3)_2$, in water, followed by treatment with sodium borohydride in sodium hydroxide solution:

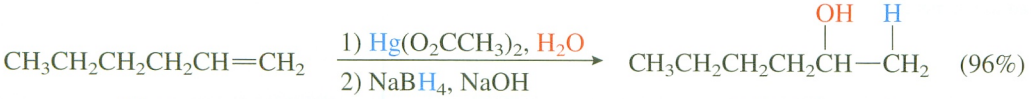


Cyclopentene Cyclopentanol

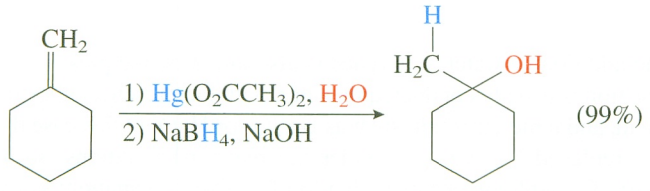
Although this reaction involves two steps, they can be run sequentially in the same flask. This procedure is usually the preferred method for the hydration of an alkene because the yields are higher than the acid-catalyzed addition described in Section 11.3, and rearrangements do not occur.

Figure 11.5 shows a mechanism that has been postulated for this reaction. First, an electrophilic mercury species adds to the double bond to form a cyclic mercurinium ion. Note how similar this mechanism is, including its stereochemistry and regiochemistry, to that shown in Figure 11.4 for the formation of a halohydrin. The initial product results from anti addition of Hg and OH to the double bond. In the second step, sodium borohydride replaces the mercury with a hydrogen with random stereochemistry. (The mechanism for this step is complex and not important to us at this time.) The overall result is the addition of H and OH with Markovnikov orientation.

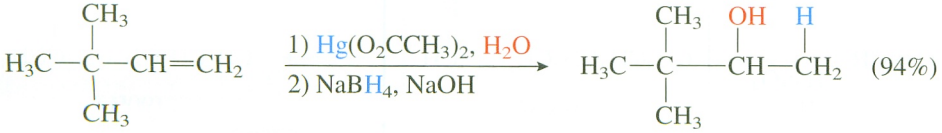
Some additional examples are provided by the following equations. Note the excellent yields in all of the examples. Also note that the last example proceeds without rearrangement because the intermediate is a mercurinium ion rather than a carbocation. Attempts to prepare this alcohol by acid-catalyzed addition of water result in completely rearranged product.



1-Hexene 2-Hexanol



Methylenecyclohexane 1-Methylcyclohexanol

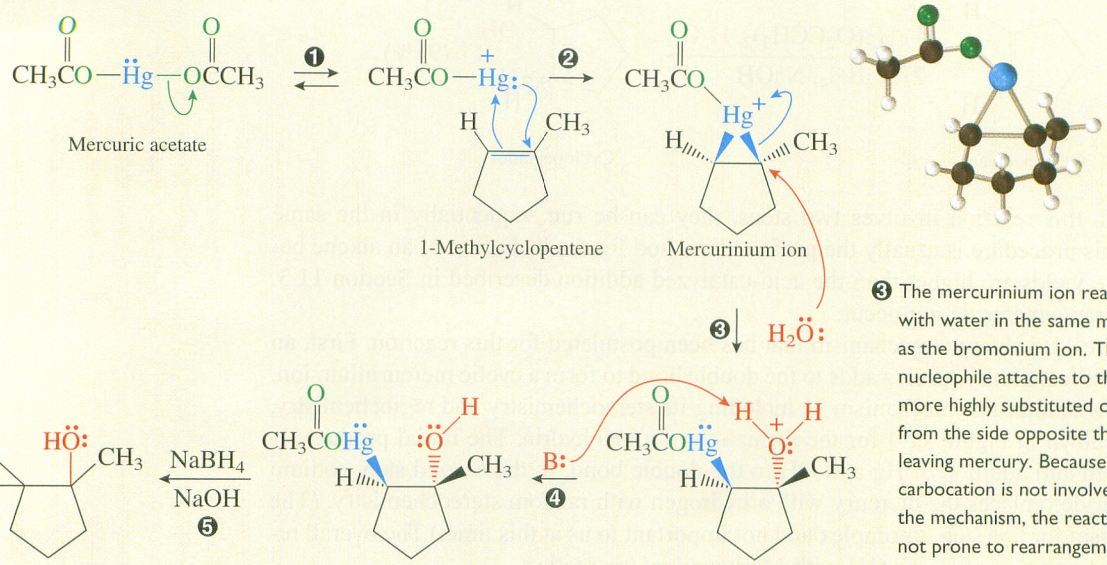


3,3-Dimethyl-1-butene 3,3-Dimethyl-2-butanol

For simplicity, mercuric acetate is shown with covalent bonds. Mercury has a filled 5*d* subshell. Two of these 5*d* unshared electrons are shown.

❶ In the first step of the reaction, acetate anion leaves to generate the mercury electrophile.

❷ The mercury electrophile adds to the double bond in a process very similar to the formation of a bromonium ion. A species called a mercurinium ion is formed.



❸ The mercurinium ion reacts with water in the same manner as the bromonium ion. The nucleophile attaches to the more highly substituted carbon from the side opposite the leaving mercury. Because a free carbocation is not involved in the mechanism, the reaction is not prone to rearrangement.

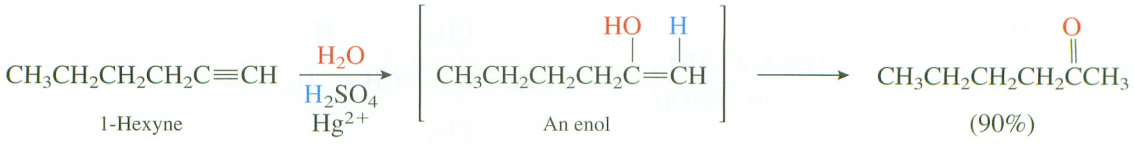
❺ Sodium borohydride replaces the mercury with a hydrogen by a complex mechanism. In this particular case, as in most cases, the stereochemistry of the overall addition no longer matters because there are now two hydrogens on the carbon that was bonded to the mercury.

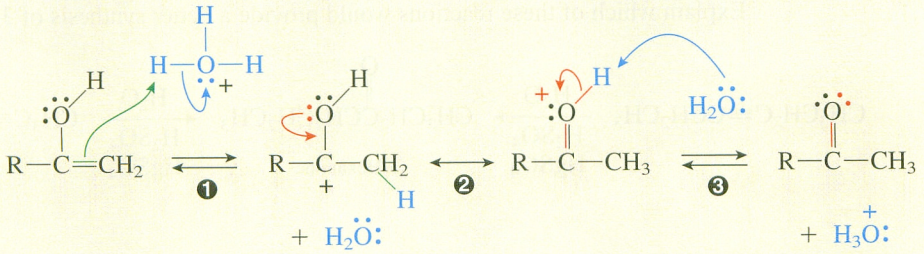
❹ A base in the solution, such as water or acetate ion, removes the proton.

Figure 11.5

MECHANISM OF THE HYDRATION OF AN ALKENE USING MERCURIC ACETATE.

The addition of water to alkynes is also aided by the presence of mercury (II) salts. The reaction is usually conducted in water, with the presence of a strong acid, such as sulfuric acid, and a mercury salt, such as $HgSO_4$ or HgO. In this case the mercury is spontaneously replaced by hydrogen under the reaction conditions, so a second step is not necessary. The addition occurs with a Markovnikov orientation; stereochemistry is not an issue.





❶ In the presence of acid the double bond of the enol gets protonated. This step of the mechanism is identical to the first step of the mechanism for addition of the hydrogen halides and the acid-catalyzed addition of water to alkenes. The addition occurs so that the positive charge is located on the carbon that is bonded to the hydroxy group because this carbocation is stabilized by resonance.

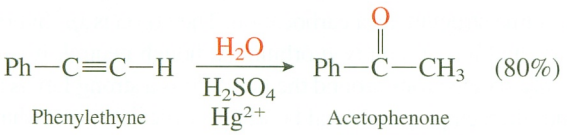
❷ The resonance structure on the right is much more stable than the one on the left because the octet rule is satisfied for all of the atoms. The cation is actually the conjugate acid of a ketone. Because this cation is so much lower in energy than the usual carbocation, the transition state leading to it is also lower in energy (Hammond postulate). Thus, it is formed readily and the initial addition of the proton is very fast.

❸ To complete the tautomerization, it is necessary only for a base, such as water, to remove the proton on the oxygen. The tautomerization is fast in both directions, but the equilibrium greatly favors the ketone tautomer.

Figure 11.6

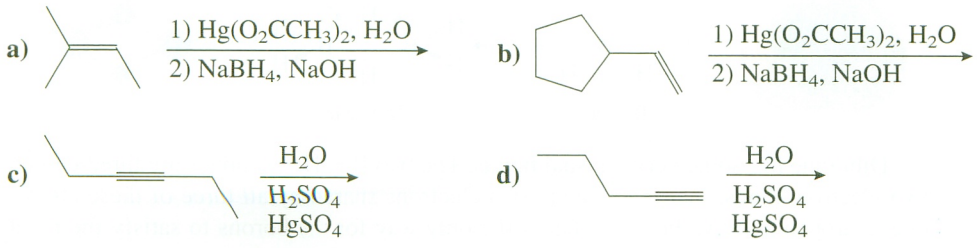
MECHANISM OF THE TAUTOMERIZATION OF AN ENOL TO A KETONE.

The initial product has a hydroxy group attached to a carbon–carbon double bond. Compounds such as this are called **enols** (ene + ol) and are very labile—they cannot usually be isolated. Enols such as this spontaneously rearrange to the more stable ketone isomer. The ketone and the enol are termed **tautomers.** This reaction, which simply involves the movement of a proton and a double bond, is called a **keto–enol tautomerization** and is usually very fast. In most cases the ketone is much more stable, and the amount of enol present at equilibrium is not detectable by most methods. The mechanism for this tautomerization in acid is shown in Figure 11.6. The mercury-catalyzed hydration of alkynes is a good method for the preparation of ketones, as shown in the following example:



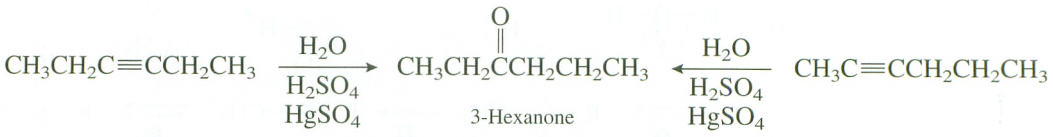
PROBLEM 11.13

Show the products of these reactions:



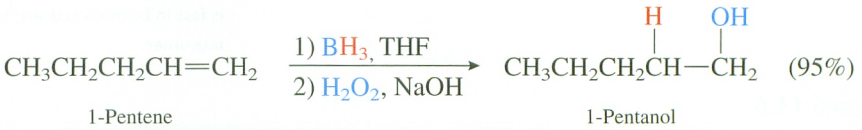
PROBLEM 11.14

Explain which of these reactions would provide a better synthesis of 3-hexanone.



11.7 HYDROBORATION–OXIDATION

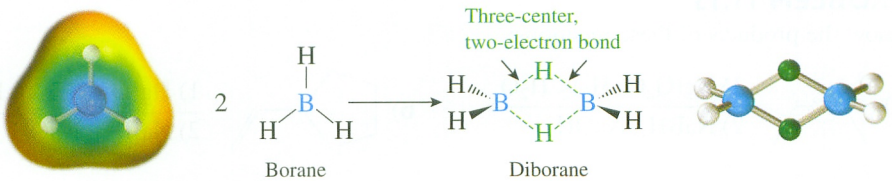
Another method for the addition of the elements of water, H and OH, to an alkene was developed by H. C. Brown, who shared the 1979 Nobel Prize in chemistry for this work. In this reaction the alkene is first allowed to react with a complex of borane (BH_3) in tetrahydrofuran (THF). The initial product is then allowed to react with a basic solution of hydrogen peroxide. An example is shown in the following equation:



The most interesting feature of this reaction is its regiochemistry. The hydrogen has added to the carbon with more alkyl groups, and the hydroxy group has added to the carbon with more hydrogens, in opposition to Markovnikov's rule. Thus, the hydroboration–oxidation reaction results in **anti-Markovnikov addition** of water to the carbon–carbon double bond. It is just this feature, the opposite regiochemistry as compared to the hydration reaction or the oxymercuration–reduction process, that makes this reaction so valuable. Now we have a choice: we can add H and OH to an alkene with either regiochemistry!

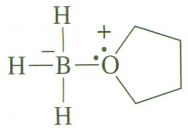
Although the hydroboration–oxidation reaction gives a product with a regiochemistry opposite to that predicted by Markovnikov's rule, the regiochemistry is in accord with the mechanistic version of this rule—that is, the electrophile adds to the less substituted carbon. Let's look at the mechanism of this reaction.

Borane has the same structure as a carbocation. The boron is sp^2 hybridized, with trigonal planar geometry, and has an empty p orbital. Although neutral, it is electron deficient because there are only six electrons around the boron. It is a strong Lewis acid. An electron-deficient compound often employs unusual bonding to alleviate somewhat its instability. In the case of borane, two molecules combine to form one molecule of diborane:



Diborane has some very unusual bonds. The two B—H—B bonds are three-center, two-electron bonds; that is, there are two electrons shared by all three of these atoms, one hydrogen and two borons. That is the only way for the borons to satisfy the octet

rule in this electron-deficient species. In tetrahydrofuran solution, borane is present as a complex with the oxygen of the tetrahydrofuran, which acts as a Lewis base.

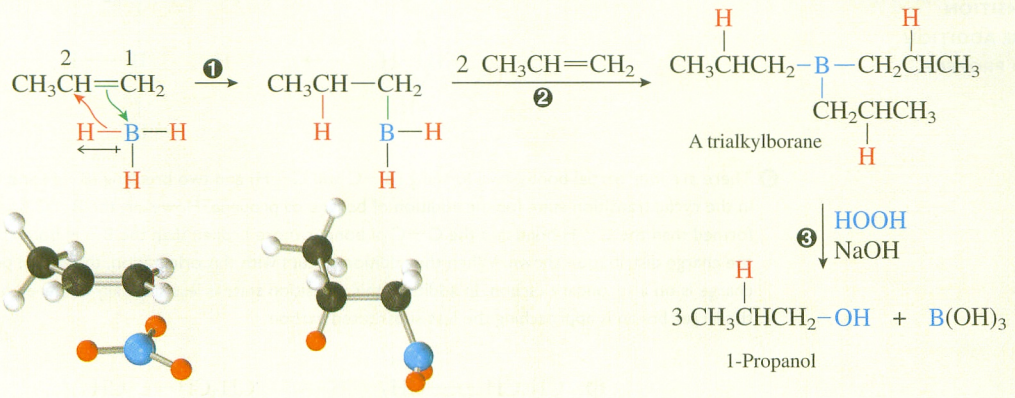


Borane–tetrahydrofuran complex

However, it is easiest to understand the hydroboration reaction by considering the reactive species to be BH_3 itself.

In the first step of the reaction, as shown in Figure 11.7, borane adds to the alkene. The reaction is initiated by the electrophilic boron reacting with the pi electrons of the carbon–carbon double bond. However, a carbocation is not formed. Instead, as positive charge begins to build up on the carbon, the hydrogen is delivered from the boron to this carbon as a nucleophile. The overall process is concerted—two bonds (C—B and C—H) are made and two bonds (B—H and C—C pi) are broken simultaneously in a cyclic, four-membered transition state (see Figure 11.8). Each of the boron–hydrogen bonds is reactive, so the process is repeated twice more to produce a trialkylborane. The second step of the reaction employs hydrogen peroxide to convert the carbon–boron bonds to carbon–oxygen bonds.

The regiochemistry of the reaction is in accord with the rule that the electrophile—the boron, in this case—adds to the carbon that is bonded to more hydrogens. The reason given previously for this orientation was that the electrophile adds so as to produce the more stable carbocation. As shown in Figure 11.7, no carbocation is involved in the



❶ Boron, with its empty *p* orbital, that acts as the electrophile. As positive charge begins to build up on C-2, the hydrogen, which has a partial negative charge because it is more electronegative than the boron, acts as a nucleophile. The C—H and C—B bonds are formed and the B—H and C—C pi bonds are broken in a single step. In accord with the mechanistic version of Markovnikov's rule, the electrophile, the boron, adds to the carbon bonded to more hydrogens.

❷ Both of the other two B—H bonds also add to alkene molecules. The overall result is that one borane molecule reacts with three alkene molecules to produce a boron attached to three alkyl groups, a trialkylborane.

❸ In the next step of the reaction, hydrogen peroxide breaks each C—B bond, replacing them with C—OH and B—OH bonds. (An understanding of the mechanism of this step is not important.)

Figure 11.7

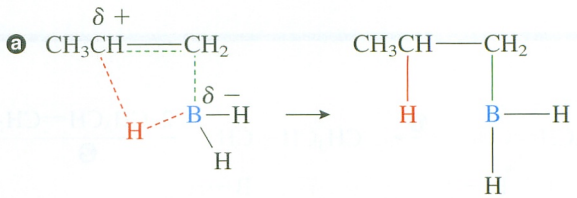
MECHANISM FOR THE HYDROBORATION OF PROPENE.

mechanism of the hydroboration reaction. Why, then, is the rule still followed? Although a fully charged carbocation is not formed in the reaction, there is some charge buildup in the transition state. The boron–carbon bond is somewhat more formed in the transition state than is the hydrogen–carbon bond. In addition, the pi bond is somewhat more broken than is the boron–hydrogen bond. As shown in Figure 11.8, this results in some negative charge buildup on the boron and some positive charge buildup on the carbon. The more stable transition state has the positive charge buildup on the carbon that can best stabilize it, the one with more alkyl substituents. To form this transition state, the electrophile must add to the carbon attached to more hydrogens. Because the charge on the carbon is less than a full unit of positive charge, the difference in the energies of the two transition states is smaller than was the case for the addition reactions that proceed through carbocation intermediates. A small amount of the reaction does proceed through the less stable transition state, and the reaction is regioselective but not regiospecific. However, the amount of the minor product is usually small enough that it can be ignored. Steric factors are also important in these reactions. Thus, the boron, being larger than the hydrogen, prefers to add to the less hindered carbon of the double bond. This steric effect favors the same transition state as the electronic factors—the less hindered carbon is the one bonded to more hydrogens.

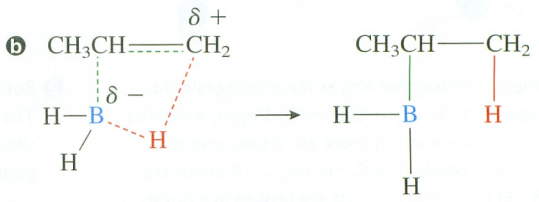
What about the stereochemistry of the reaction? Because the boron and the hydrogen are bonded to each other, in a concerted reaction they must add in a syn manner. There is no way that the boron could add to one side of the double bond and the hydrogen bonded to it could add to the other side. However, of more concern to us is the stereochemistry of the hydroxy group. The hydroxy group replaces the boron with complete retention of con-

Figure 11.8

POSSIBLE TRANSITION STATES FOR THE ADDITION OF BORANE TO PROPENE.



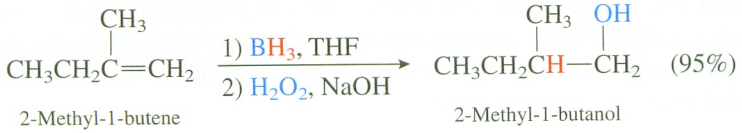
a There are four partial bonds, two forming (B—C and C—H) and two breaking (B—H and C—C pi) in the cyclic transition state for the addition of borane to propene. However, the B—C bond is more formed than the C—H bond and the C—C pi bond is more broken than the B—H bond, resulting in the charge distribution shown. When the addition occurs with this orientation, the partial positive charge is on a secondary carbon. In addition, this transition state is less sterically hindered because the larger boron is approaching the less substituted carbon.



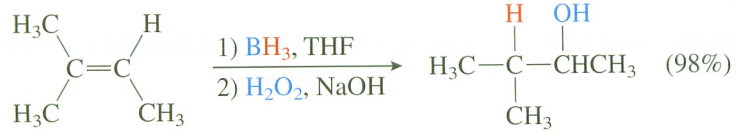
b When the addition occurs with this orientation, the partial positive charge is on a primary carbon. The charge is less stabilized here than in case **a**, so this transition state is less favorable than that of case **a**. This transition state is also less favorable for steric reasons.

The difference in transition state energies is enough that most of the reaction follows the orientation of case **a** where the electrophile has added to the carbon attached to more hydrogens. Although some of the product is formed by the orientation of case **b**, the amount is small enough that it can be ignored for most purposes.

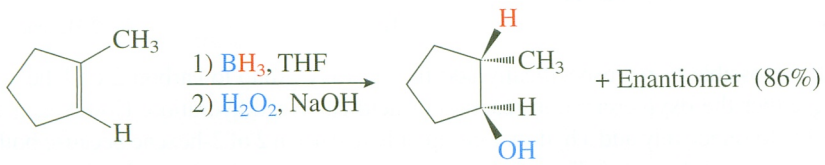
figuration. Therefore, the reaction occurs in a regioselective and stereospecific manner: the H and the OH are added with anti-Markovnikov orientation and syn stereochemistry. Some illustrative examples are provided in the following equations. Pay particular attention to both the regiochemistry and the stereochemistry in the last example.



2-Methyl-1-butene — 2-Methyl-1-butanol



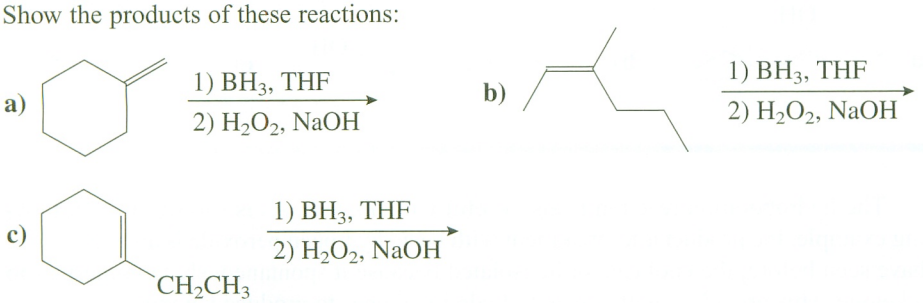
2-Methyl-2-butene — 3-Methyl-2-butanol



1-Methylcyclopentene — *trans*-2-Methylcyclopentanol

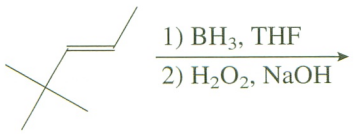
PROBLEM 11.15

Show the products of these reactions:



PROBLEM 11.16

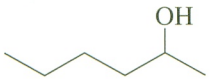
This hydroboration reaction forms two products. Show these products and explain which one you expect to be major.



ORGANIC Chemistry Now™
Click *Coached Tutorial Problems* for more practice with the **Hydroboration of Alkenes.**

PRACTICE PROBLEM 11.4

Show how to prepare this alcohol from an alkene:

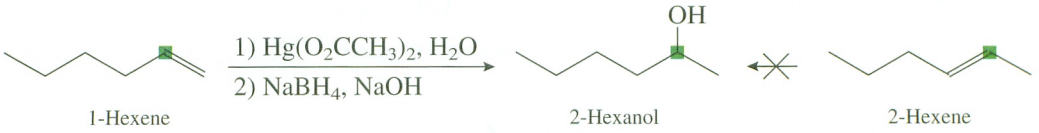


Strategy

The hydroxy group must be located on one of the doubly bonded carbons of the original alkene, so first draw all of the alkenes that meet this criterion. Examine the alkenes to determine whether it is possible to selectively add the OH group to the desired carbon. Remember that we can add the OH with either Markovnikov orientation (acid-catalyzed hydration or oxymercuration–reduction) or anti-Markovnikov orientation (hydroboration–oxidation), but we will have difficulty selecting between two carbons that are similarly substituted.

Solution

The two alkenes that could potentially be used to prepare 2-hexanol are 1-hexene and 2-hexene:

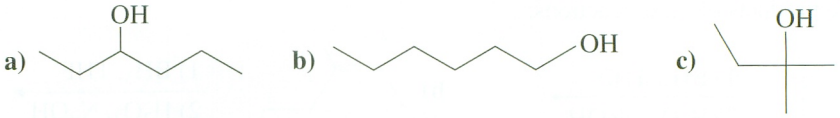


1-Hexene 2-Hexanol 2-Hexene

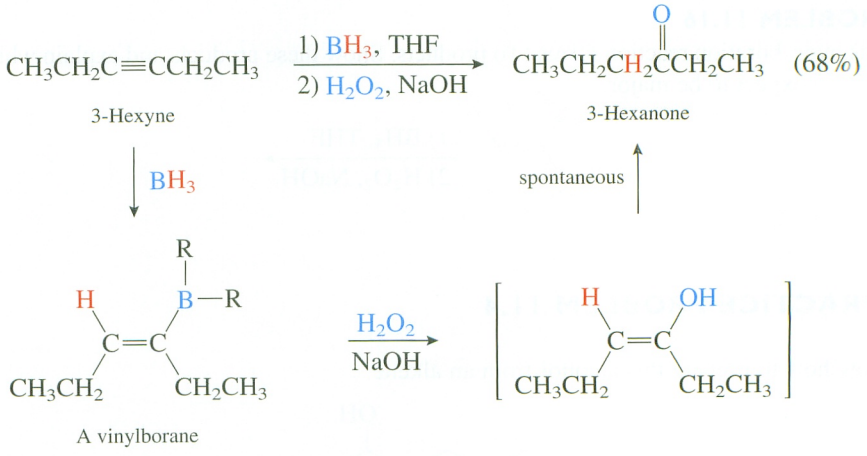
It is possible to regiospecifically add the hydroxy group to carbon 2 of 1-hexene by using either the oxymercuration reaction or acid-catalyzed hydration. However, it is not possible to selectively add a hydroxy group only to carbon 2 of 2-hexene because both carbons are monosubstituted. Therefore, the path starting from 1-hexene should be used.

PROBLEM 11.17

Show preparations of these alcohols from alkenes.



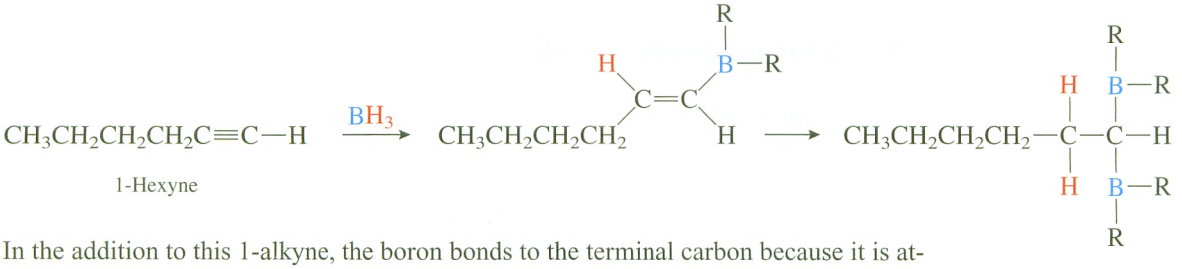
The hydroboration reaction is also useful with alkynes. As is shown in the following example, the product after treatment with basic hydrogen peroxide is an enol. As we have seen before, the enol cannot be isolated because it spontaneously tautomerizes to a ketone. This provides another way to hydrate alkynes to produce ketones.



A vinylborane

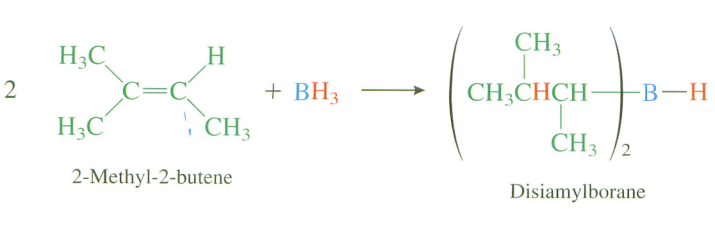
As mentioned previously, the addition of borane, or an alkyl-substituted borane, to a carbon–carbon double bond is very sensitive to steric hindrance. The preceding vinylborane does not add a second boron because of the steric bulk of the ethyl group and the boron group on the end of the double bond. If the boron is considered to be about the same size as a carbon, then this vinylborane corresponds to a trisubstituted alkene.

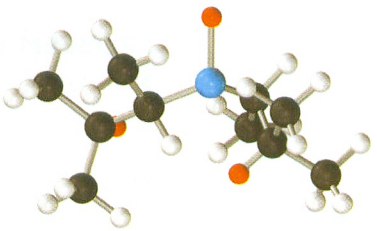
3-Hexyne has the triple bond in the middle of a carbon chain and is termed an internal alkyne. If, instead, an alkyne with the triple bond at the end of the carbon chain, a 1-alkyne or a terminal alkyne, were used in this reaction, then the reaction might be useful for the synthesis of aldehydes. The boron is expected to add to the terminal carbon of a 1-alkyne. Reaction with basic hydrogen peroxide would produce the enol resulting from anti-Markovnikov addition of water to the alkyne. Tautomerization of this enol would produce an aldehyde. Unfortunately, the vinylborane produced from a 1-alkyne reacts with a second equivalent of boron as shown in the following reaction. The product, with two borons bonded to the end carbon, does not produce an aldehyde when treated with basic hydrogen peroxide.



In the addition to this 1-alkyne, the boron bonds to the terminal carbon because it is attached to more hydrogens. The resulting vinylborane can be viewed as a disubstituted alkene and is less hindered than the vinylborane produced from an internal alkyne (a trisubstituted alkene). Because the vinylborane is less hindered, it adds a second boron to produce an alkane substituted on the end carbon with two boron groups.

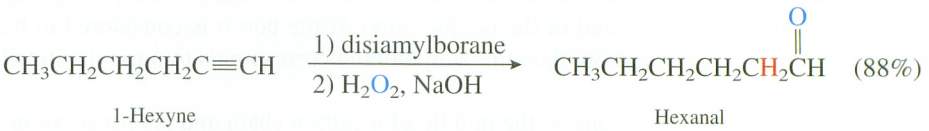
If the hydroboration reaction is to be used to convert 1-alkynes into aldehydes, some way to stop the addition at the vinylborane stage is needed. The problem is that there is not enough steric hindrance at the end carbon of the vinylborane. The solution is to build extra steric hindrance into the other alkyl groups attached to the boron of the vinylborane. A borane, R_2BH, with two bulky R groups already attached to the boron is used as the hydroboration reagent. One such reagent is prepared by the reaction of two equivalents of 2-methyl-2-butene (also known by the common name of isoamylene) with borane to produce a dialkylborane called disiamylborane (a shortened version of diisoamylborane):





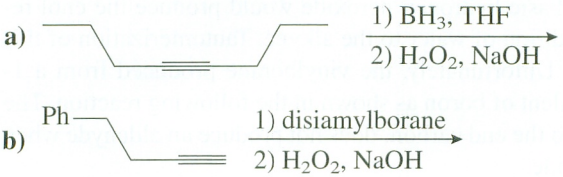
Once there are two of the bulky alkyl groups attached to the boron, it is difficult to add a third group. Disiamylborane is not reactive enough to add to isoamylene, a trisubstituted alkene, because of these steric effects. However, it is reactive enough to add to a 1-alkyne to produce a vinylborane, but it is too sterically hindered to react with the

vinylborane product. Oxidation of the vinylborane with basic hydrogen peroxide produces an aldehyde in excellent overall yield, as shown in the following example:



PROBLEM 11.18

Show the products of these reactions:

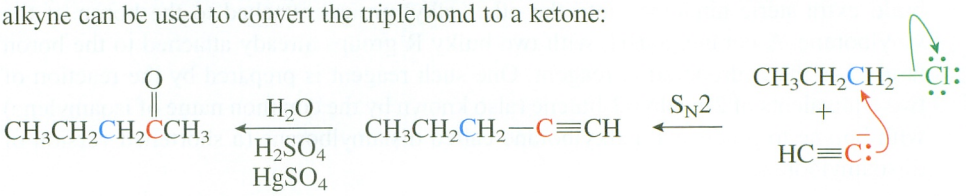


PRACTICE PROBLEM 11.5

Show a synthesis of 2-pentanone from 1-chloropropane:

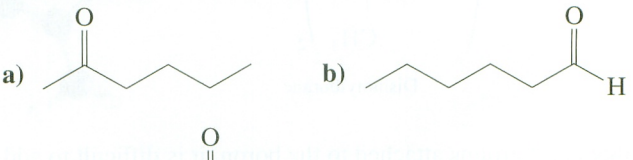
Solution

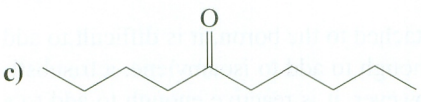
Remember to work backward. The target ketone has five carbons, whereas the designated starting material has only three, so it is necessary to form a carbon–carbon bond. A nucleophilic substitution reaction can be done at C-1 of 1-chloropropane, so a two-carbon nucleophile that can be ultimately converted to a ketone is required. A carbon–carbon bond-forming reaction that meets these requirements is the alkylation of an acetylide anion (see Section 10.8). Once the carbon–carbon bond has been formed, hydration of the alkyne can be used to convert the triple bond to a ketone:



PROBLEM 11.19

Show syntheses of these compounds from 1-bromobutane:

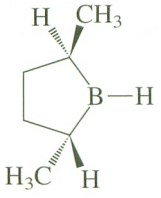




Focus On

Chiral Boranes in Organic Synthesis

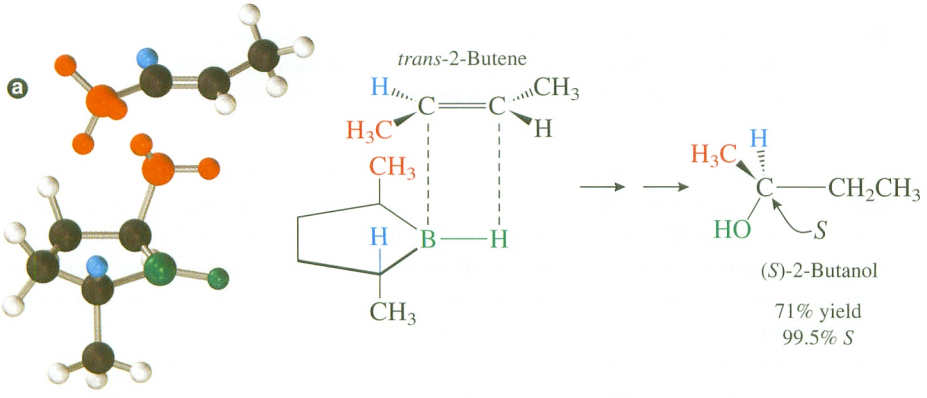
As we saw in Chapter 7, one of the goals of synthetic organic chemistry is to develop methods that produce only a single enantiomer of a desired chiral compound rather than the usual racemic mixture that is the result of most reactions. Recently, a method has been developed that employs one enantiomer of a chiral borane to prepare a single enantiomer of a chiral alcohol from an achiral alkene. The chiral borane that is used is *trans*-2,5-dimethylborolane.



trans-2,5-Dimethylborolane

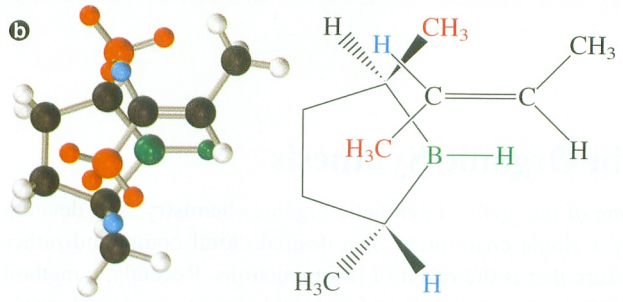
The stereoisomer of *trans*-2,5-dimethylborolane shown here has the *R* configuration at both stereocenters. Reaction of this chiral borane with *trans*-2-butene produces 2-butanol in 71% yield. The 2-butanol is almost enantiomerically pure. It consists of 99.5% of the (*S*)-enantiomer and only 0.5% of the (*R*)-enantiomer. This occurs because the transition state leading to the (*S*)-enantiomer is much more favorable on steric grounds than is the transition state leading to the (*R*)-enantiomer.

The approach of *trans*-2-butene to the chiral borane is shown in the following diagram.

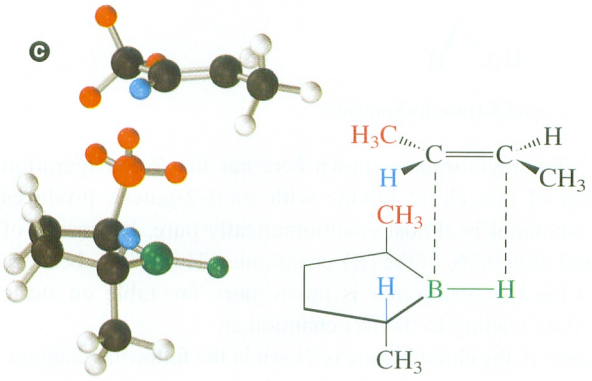


a The blue hydrogen of the alkene interacts with the red methyl group of the borane while the red methyl group of the alkene interacts with the blue hydrogen of the borane. This geometry minimizes the steric repulsions as the molecules approach to form the transition state. After oxidation of the carbon–boron bond to a carbon–oxygen bond, which occurs with retention of configuration, 2-butanol is produced in 71% yield. The reaction is remarkably selective. The product is almost entirely (*S*)-2-butanol (99.5%). It is contaminated with only a very small amount (0.5%) of the enantiomeric (*R*)-2-butanol.

Continued



b This is another view of the geometry of the reaction, with the alkene approaching from above the borane. Again it can be seen that the steric interactions between the borane and the alkene are minimized in this approach; the smaller group on the alkene (the blue hydrogen) interacts with the larger group on the borane (the red methyl) and the larger group on the alkene (the red methyl) interacts with the smaller group (the blue hydrogen) on the borane.



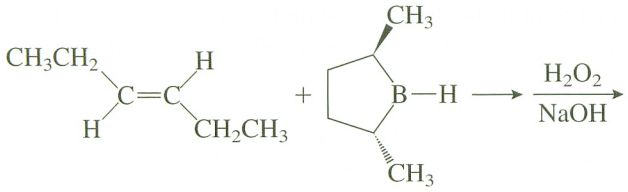
c This approach would lead to the product that is not formed, (*R*)-2-butanol. It is much less sterically favorable than **a** because the larger groups (the red methyl groups) on the alkene and the borane are interacting and hinder the formation of the transition state.

As we have seen, the hydroboration reaction is very sensitive to steric effects. The chiral borane approaches the alkene in such a manner as to minimize steric interactions. As shown in **a**, the transition state that leads to (*S*)-2-butanol has fewer, steric interactions than the transition state in **c** that leads to (*R*)-2-butanol. The overall selectivity of the reaction is very high; the product is almost entirely the (*S*)-enantiomer. Note that, to be successful in producing a single enantiomer of the product, the borane must be enantiomerically pure. Any of the (*S*,*S*)-enantiomer that is present in the borane will result in the formation of an equal amount of the other enantiomer of 2-butanol, the (*R*)-enantiomer in this case.

This reaction meets one of the criteria of a successful chiral synthesis; that is, it produces the product in high enantiomeric purity. Its drawback is that the chiral borane must be prepared and resolved, a somewhat laborious and expensive process. A more ideal process would employ the chiral reagent as a catalyst in a reaction that produces the desired product in high enantiomeric purity but requires the investment of only a small amount of the expensive chiral reagent (see the Focus On box on asymmetric hydrogenation later in this chapter).

PROBLEM 11.20

Show the product of this reaction:

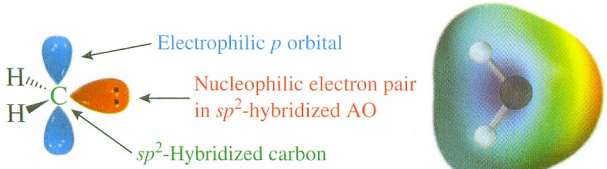


PROBLEM 11.21

Explain how a similar hydroboration reaction could be used to prepare (*R*)-2-butanol in good enantiomeric excess.

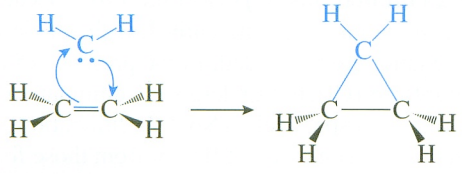
11.8 Addition of Carbenes

A **carbene** is a reactive species having a carbon with only two bonds and an unshared pair of electrons. It is quite unstable and, like a carbocation, exists only as a transient intermediate in certain reactions. The simplest carbene, CH_2, is called methylene. It is sp^2 hybridized. The unshared pair of electrons occupies one of the sp^2-hybridized AOs and the other two are used to form the bonds to the hydrogens. The remaining AO on the carbon is an unoccupied *p* orbital.



Methylene

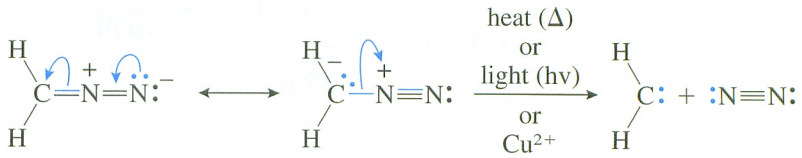
The empty *p* orbital is electrophilic, and the unshared pair of electrons is nucleophilic. A carbene resembles both the electrophilic bromine that we encountered in the addition of Br_2 to alkenes and the electrophilic mercury species that we encountered in the oxymercuration reaction in that it has both an electrophilic site (an empty orbital) and a nucleophilic site (an unshared electron pair) on the same atom. Recall that both of these species reacted as both electrophile and nucleophile, forming three-membered rings—a bromonium ion and a mercurinium ion, respectively. It is not surprising, then, that a carbene also forms a three-membered ring, a cyclopropane. However, because the ring is not charged in this case, the reaction stops at this stage, rather than continuing by reaction with a nucleophile:



Cyclopropane

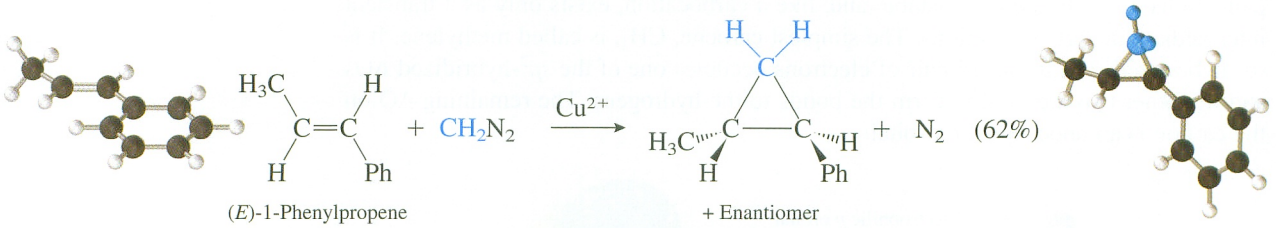
Of course, because the electrophile and the nucleophile are the same atom, the addition must proceed in a syn manner.

How are these reactive carbene species generated? Two groups must be removed from a tetravalent carbon, leaving behind one pair of electrons. We will examine three of the more important methods that accomplish this. The first is the elimination of N_2 from diazo compounds. The simplest diazo compound is diazomethane:



Diazomethane

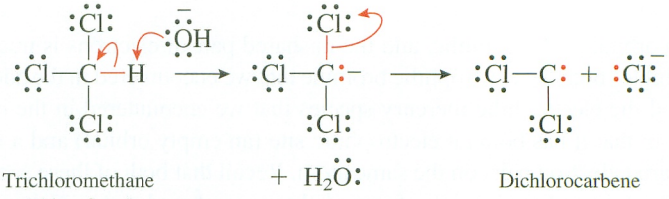
Diazo compounds are relatively unstable and readily eliminate nitrogen to form carbenes. The loss of the stable N_2 molecule provides the driving force for the formation of the high-energy carbene. The elimination can be induced by heating, by irradiation with light, or by the presence of certain metal cations, such as Cu^{2+}. If the carbene is produced in the presence of an alkene, a cyclopropane ring is produced as shown in the following example. Note the stereochemistry of the product.



(*E*)-1-Phenylpropene + Enantiomer

trans-1-Methyl-2-phenylcyclopropane

A second method to generate a carbene is to eliminate a proton and a leaving group, such as chloride or bromide ion, *from the same carbon:*

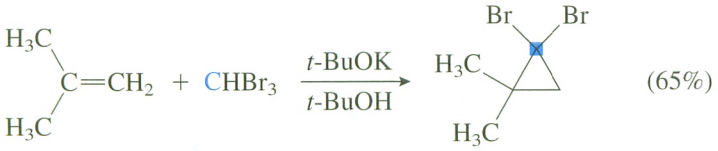


Trichloromethane (chloroform)

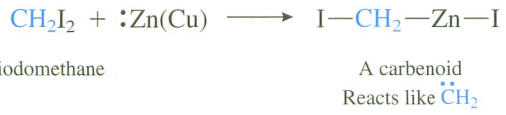
Dichlorocarbene

Such a reaction is termed a **1,1-elimination** (or an ***α*-elimination**) because both groups are removed from the same carbon. (The eliminations to produce alkenes, discussed in Chapter 9, are called **1,2-eliminations** or ***β*-eliminations.**) Because they give carbenes as products, these 1,1-eliminations are inherently less favorable than 1,2-eliminations and occur only when the latter are precluded. In the presence of a strong base, chloroform ($CHCl_3$) and bromoform ($CHBr_3$) undergo 1,1-elimination to produce dichlorocarbene and dibromocarbene, respectively. (No 1,2-elimination is possible with these compounds.) The mechanism is somewhat different from those for the 1,2-eliminations that were presented in Chapter 9 in that first the proton is removed and then the halide leaves. The electron-withdrawing effect of the halogens makes the hydrogen acidic enough to be removed by a strong base such as hydroxide or alkoxide ion. A halide ion then acts as a leaving group from the conjugate base, producing the carbene. If the car-

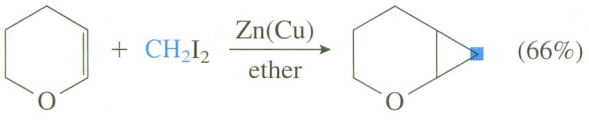
bene is generated in the presence of an alkene, a cyclopropane derivative is produced, as shown in the following examples:

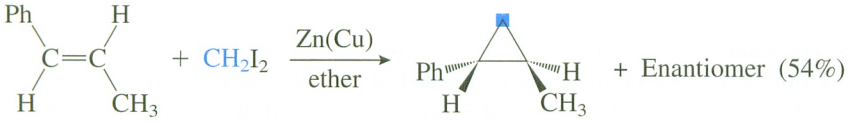


Another reaction that builds a cyclopropane ring onto a carbon–carbon double bond is called the **Simmons-Smith reaction.** This reaction does not actually involve a carbene, but rather a **carbenoid,** an organometallic species that reacts like a carbene. This species is generated by reaction of diiodomethane with zinc metal from a special alloy of zinc and copper:



The mechanism for the formation of this carbenoid and for its reaction with alkenes need not concern us here. Just remember that it reacts as though it is methylene. The Simmons-Smith reaction is an excellent way to prepare cyclopropane derivatives from alkenes, as shown in the following examples. Note the stereochemistry in the second equation.

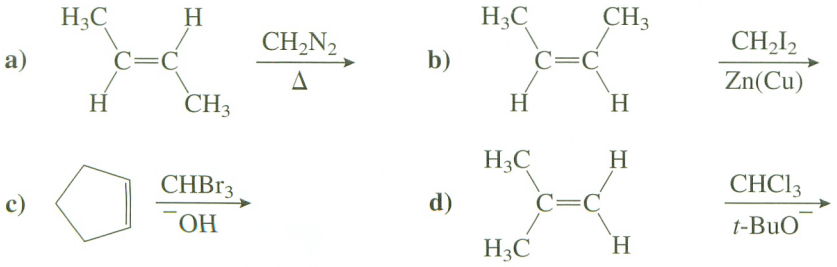




The reactions of carbenes with alkenes, as illustrated in this section, are the best methods for the synthesis of cyclopropanes.

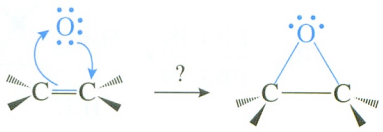
PROBLEM 11.22

Show the products of these reactions:



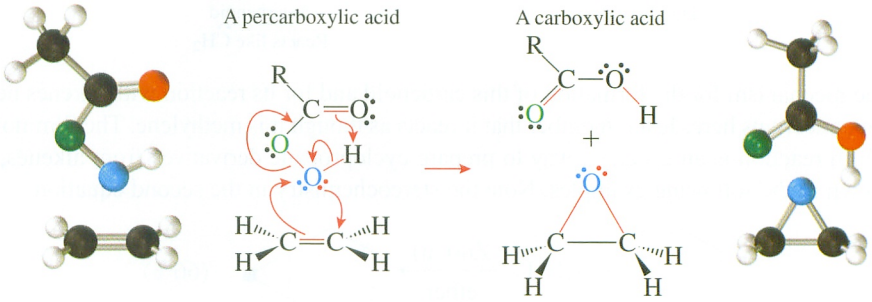
11.9 EPOXIDATION

An oxygen atom is analogous to a carbene in that it has only six electrons in its valence shell. Like a carbene, it might be expected to act as both an electrophile and a nucleophile in its reaction with an alkene, resulting in the formation of a three-membered ring containing an oxygen—an epoxide.



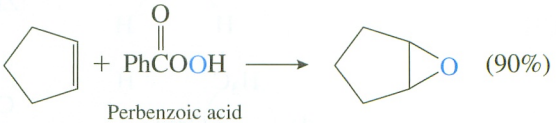
An epoxide

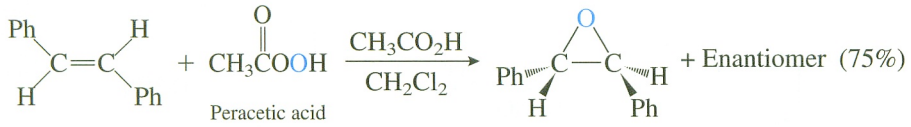
Although bottles of oxygen atoms are not available in the laboratory, **percarboxylic acids** are reagents that are able to accomplish this transformation. Recall that hydrogen peroxide, H—O—O—H, has an oxygen–oxygen bond. A percarboxylic acid also has an oxygen–oxygen bond and can act as a source of electrophilic oxygen when reacting with an alkene. The product of this reaction is an epoxide.

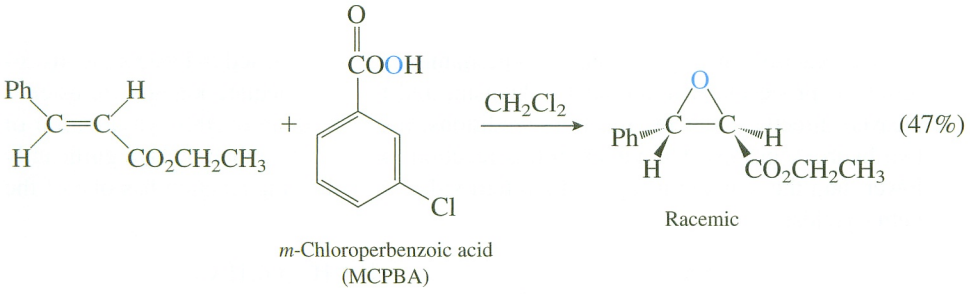


This epoxidation reaction is concerted. It appears quite complex because of all the bonds that are being made or broken in this one step. It might help to focus on the blue oxygen and imagine the process to occur in a stepwise fashion. A 1,1-elimination of the proton and the green oxygen would generate a normal carboxylic acid and an oxygen atom. Addition of the oxygen atom electrophile to the alkene, as illustrated previously, would then produce the epoxide. All of this simply happens in a single step.

Examination of this mechanism suggests that the nature of the R group should not make much difference in the reaction. In fact, a number of different percarboxylic acids can be used to epoxidize alkenes, as illustrated in the following examples. As expected, the additions occur with syn stereochemistry.

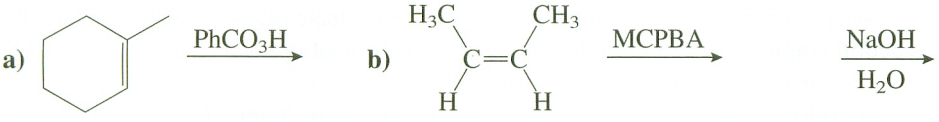






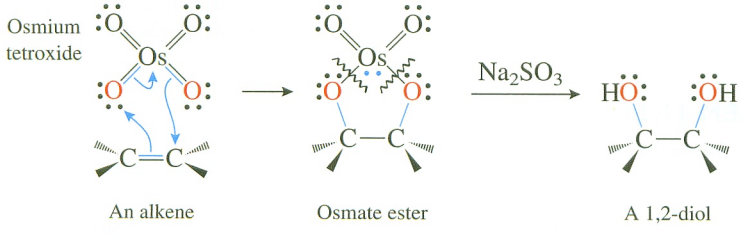
PROBLEM 11.23

Show the products of these reactions:

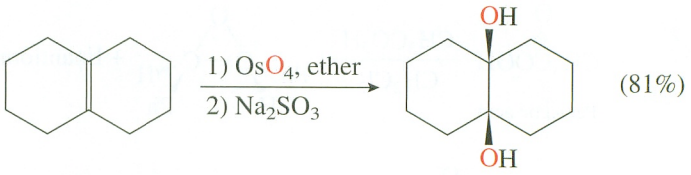


11.10 HYDROXYLATION

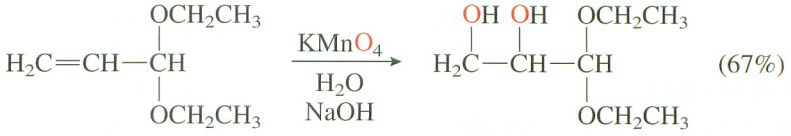
There are two reagents that add hydroxy groups to both carbons of a carbon–carbon double bond: osmium tetroxide, OsO_4, and potassium permanganate, $KMnO_4$. These operate through similar mechanisms in which one of the oxygens that is bonded to the metal acts as an electrophile and another acts as a nucleophile, as illustrated in the following equation for the reaction of osmium tetroxide:



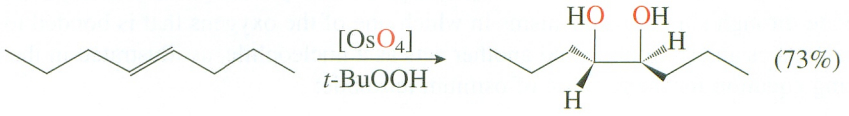
The cyclic intermediate, called an osmate ester, is not isolated; instead, the osmium–oxygen bonds are cleaved by using a reagent such as sodium sulfite, Na_2SO_3, resulting in the formation of a 1,2-diol. (The mechanistic details of the cleavage step need not concern us.) Because both the electrophilic and nucleophilic oxygens are attached to the same metal atom, both are delivered from the same side of the plane of the double bond—the reaction is a syn addition.



The reaction employing potassium permanganate is conducted in basic aqueous solution. It proceeds by a similar mechanism, and the intermediate manganate ester is cleaved directly under the reaction conditions, resulting in an overall syn addition of two hydroxy groups. The yields in this reaction are often less than 50%, significantly lower than the reaction using osmium tetroxide. The following reaction has one of the better yields:



Whereas hydroxylation using potassium permanganate often gives low yields, the reaction employing osmium tetroxide has its own limitations. The osmium reagent is very expensive and extremely toxic. To help alleviate these problems, methods have been developed that require only a catalytic amount of osmium tetroxide in the presence of some additional oxidizing agent, such as *tert*-butyl peroxide. The reaction proceeds to the cyclic osmate ester as before. The peroxide serves to cleave the ester to the diol and, importantly, oxidizes the osmium back to the tetroxide so that the cycle can be repeated. Therefore, only a small amount of osmium tetroxide is needed. The yields are respectable, as shown in the following example. Note the stereochemistry of the product.

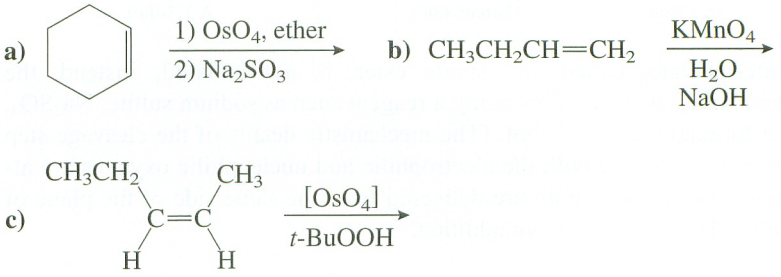


(*E*)-4-Octene

Racemic
(*d,l*)-4,5-Octanediol

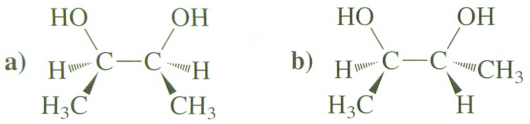
PROBLEM 11.24

Show the products of these reactions:



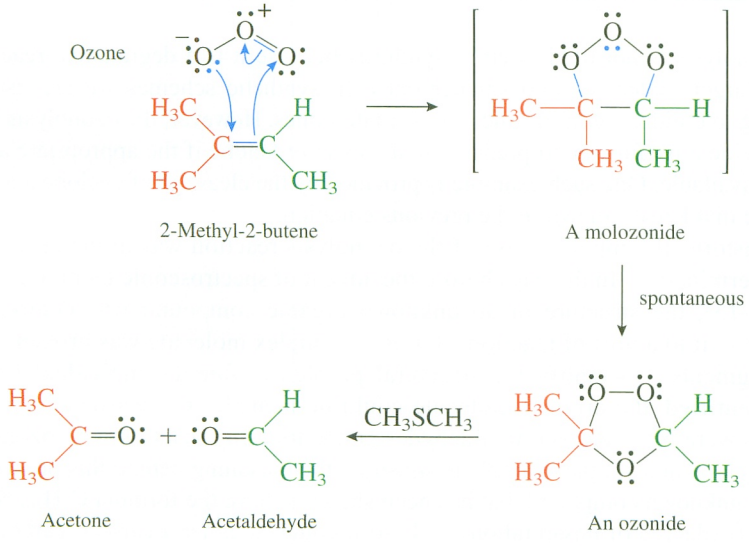
PROBLEM 11.25

Show syntheses of these compounds from (*Z*)-2-butene:

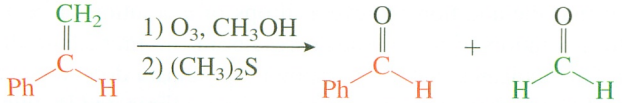


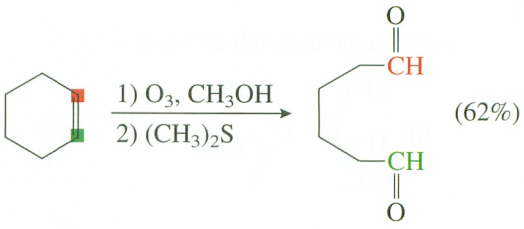
11.11 OZONOLYSIS

Ozone, O_3, is a form of oxygen found in the upper atmosphere. Its presence there is beneficial because it absorbs some harmful ultraviolet radiation, preventing it from reaching the surface of the earth. Ozone is also found at the surface of the earth as a component of smog. Here, its presence is detrimental because of its high reactivity. One of the important reactions of ozone occurs with alkenes and results in the cleavage of the carbon–carbon double bond as illustrated in the following example. The ozone first adds to the double bond. This addition can be viewed as though one oxygen atom acts as an electrophile and the other acts as a nucleophile, although the mechanism is actually an example of a pericyclic reaction (see Chapter 22). The initial product, called a molozonide, spontaneously rearranges to an ozonide. The ozonide is not usually isolated. Instead, it is treated with a reducing agent (dimethyl sulfide works nicely) that cleaves the O—O bond and results in the formation of two carbonyl groups. This sequence results in the cleavage of the carbon–carbon double bond and the formation of two carbon–oxygen double bonds.



Some examples are shown in the following equations:

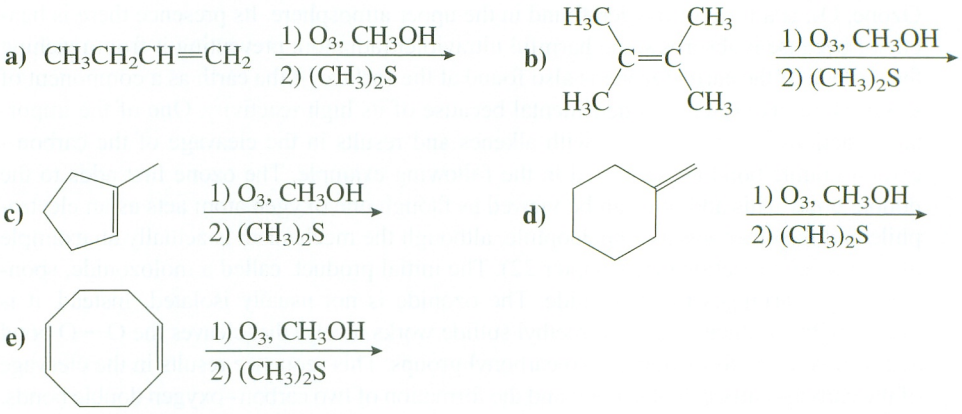




(62%)

PROBLEM 11.26

Show the products of these reactions:



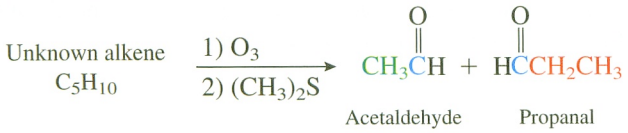
Ozonolysis is not used often in synthesis because it is a degradative reaction—it breaks larger molecules into smaller ones. In synthetic schemes we are usually attempting to build larger molecules from smaller ones. However, the ozonolysis reaction can provide a useful way to prepare an aldehyde or ketone if the appropriate alkene is readily available. One such example is provided by the cleavage of cyclohexene to produce the dialdehyde shown in the previous equation.

A historically important use of the ozonolysis reaction was in the area of structure determination. In the days before the advent of spectroscopic techniques (Chapters 13–15), the structure of an unknown organic compound was determined by submitting it to a host of reactions. Often, a complex molecule was broken into several fragments to simplify the structural problem. After the individual fragments were identified, the original molecule could be mentally reconstructed from them. Alkenes were often cleaved to aldehydes and ketones by reaction with ozone.

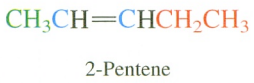
Let's look at a simple example to illustrate the reasoning behind this process. Consider an unknown compound that has been shown to have the formula C_5H_{10}. Note that it has DU (degree of unsaturation) = 1, so it contains either a carbon–carbon double bond or a ring. How could we determine which of these two structural features is present? One way to do this is to use the test described in Section 11.4. When the test is conducted, we find that the addition of several drops of a solution of bromine in carbon tetrachloride to a solution of the unknown results in the immediate discharge of the bromine color. This indicates that the compound contains a double bond. Although all of the isomers of C_5H_{10} that contain a ring have been eliminated by this test, there are still five isomeric alkenes with this formula.

The next step is to react the unknown alkene with ozone, followed by treatment with dimethyl sulfide. The products of this reaction are isolated and identified (by other

chemical tests and their physical properties) as the two aldehydes shown in the following equation:



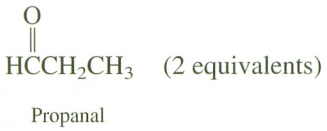
Now we must apply some reverse reasoning. What alkene will produce these two aldehydes upon cleavage with ozone? The two carbons of the carbonyl groups of these aldehydes (the blue carbons) must have been doubly bonded together in the original alkene. Therefore, the unknown alkene must be 2-pentene:



The problem is not quite completed, because we still do not know whether the original alkene was the *cis*- or *trans*-isomer of 2-pentene. More information is needed to answer this question.

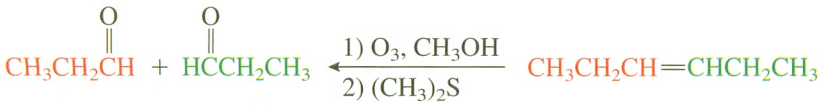
PRACTICE PROBLEM 11.6

What alkene would produce 2 equivalents of propanal upon ozonolysis?



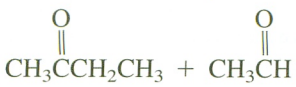
Solution

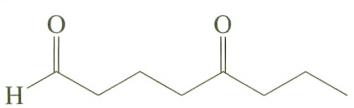
The ozonolysis reaction cleaves the carbon–carbon double bond into two carbonyl groups. In working backward from the carbonyl compounds to the alkene that produces them, just connect the two carbons of the carbonyl groups by a double bond. Because 2 equivalents of the aldehyde are formed in this example, the two carbonyl compounds are the same. The original alkene was the symmetrical 3-hexene. Of course, we have no way of determining whether it was the *E* or the *Z* stereoisomer on the basis of this information.



PROBLEM 11.27

Show the alkenes that produce these compounds on ozonolysis:

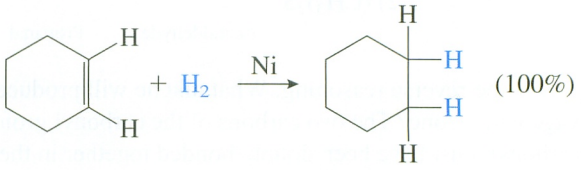
a) 

b) 

c) 

11.12 CATALYTIC HYDROGENATION

The reaction of an alkene with hydrogen in the presence of a metal catalyst results in the addition of hydrogen to the carbon–carbon double bond.



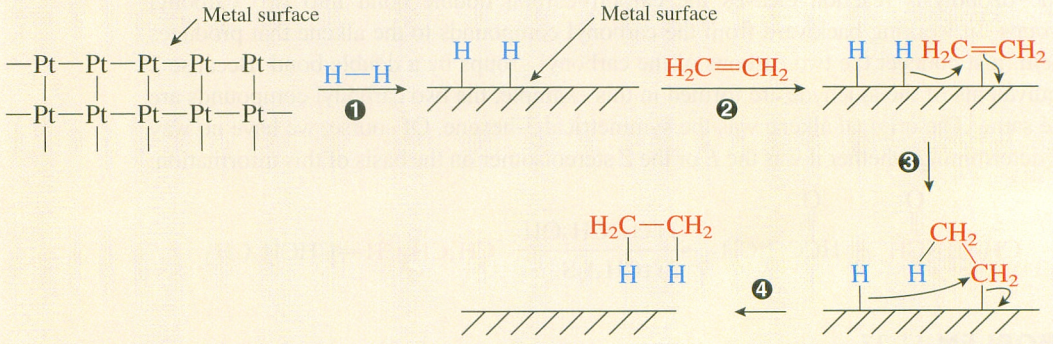
Dihydropyran Tetrahydropyran

The catalysts that are commonly used for this reaction are the members of the nickel group: nickel, palladium, and platinum. Although nickel is sometimes used, as in the previous example, palladium and platinum usually work better.

This reaction does not involve an electrophilic addition to the alkene and, technically, does not belong in this chapter. However, it is convenient to include it here because it does result in addition to the alkene. The reaction occurs on the surface of the metal, so the catalyst must be present in a very finely divided or powdered state to maximize its surface area. A simplified version of the reaction mechanism on a platinum catalyst is presented in Figure 11.9. The unused valences of the atoms at the surface of the metal are used to break the hydrogen–hydrogen bonds, forming metal–hydrogen

❶ The atoms at the surface of any metal have unused bonding capability (or valence) that can be used to form bonds to other species that approach the surface. For example, when H_2 molecules adsorb to the surface of platinum, the H—H bond is broken and the hydrogen atoms form bonds to the platinum atoms.

❷ Likewise, an alkene can form a complex with the atoms at the metal surface, using the *p* orbitals of its pi bond.



❹ A second hydrogen is transferred to the other carbon. Because no bond exists between them anymore, the alkane product diffuses away from the metal surface so that the surface is available to repeat the cycle.

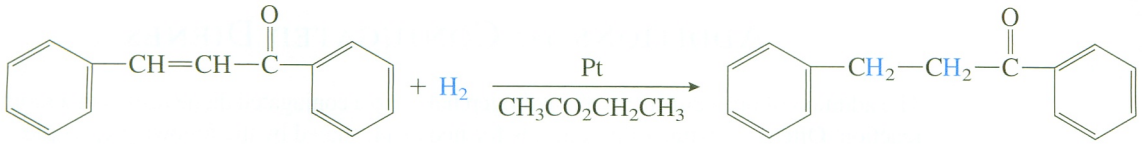
❸ A hydrogen atom is then transferred to one carbon of the alkene. Now there is an alkyl group bonded to the metal surface.

Figure 11.9

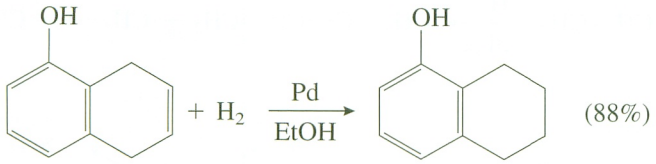
MECHANISM OF THE CATALYTIC HYDROGENATION OF AN ALKENE.

bonds, and to complex with the carbon–carbon pi bonds of the alkene. The hydrogens are then transferred to the carbons, and the newly produced alkane detaches from the surface so that the metal atoms are free to repeat the process. The stereochemistry of the addition to alkenes only makes a difference when the alkene is substituted with four alkyl groups—that is, with tetrasubstituted alkenes. In such cases the major product is found to be the one resulting from syn addition, although the reaction is seldom completely stereospecific. This is consistent with a mechanism by which both hydrogens attach to the side of the double bond that initially bonds to the metal surface.

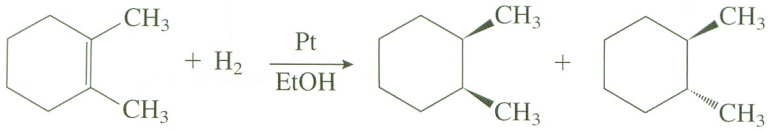
When the catalytic hydrogenation reaction is run under relatively mild conditions (room temperature and a pressure of hydrogen gas of several atmospheres or less), the reaction is very selective. Carbon–carbon double bonds of alkenes and carbon–carbon triple bonds of alkynes react readily, whereas carbon–carbon double bonds of aromatic rings and carbon–oxygen double bonds are usually inert under these reaction conditions. Some examples are provided in the following equations. Note that the stereochemistry of the addition reaction makes no difference in the first two examples. In the last example the major product results from syn addition.



(95%)

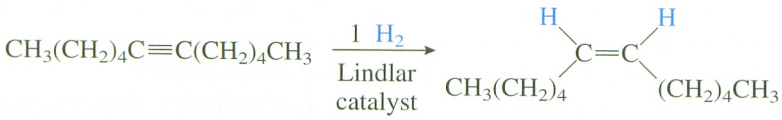


(88%)



Major Minor

Alkynes normally react with two equivalents of hydrogen to produce alkanes. However, it is also possible to react an alkyne with only one equivalent of hydrogen and stop the reaction at the alkene stage if a special catalyst, called Lindlar catalyst, is used. The Lindlar catalyst is a deactivated form of palladium that is less reactive than normal catalysts. This method provides good yields of the *cis*-alkene, resulting from syn addition of hydrogen:

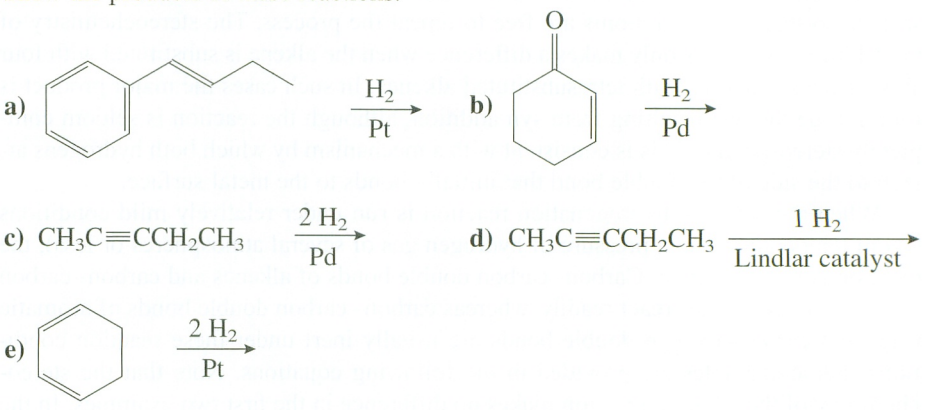


(87%)

A *cis*-alkene

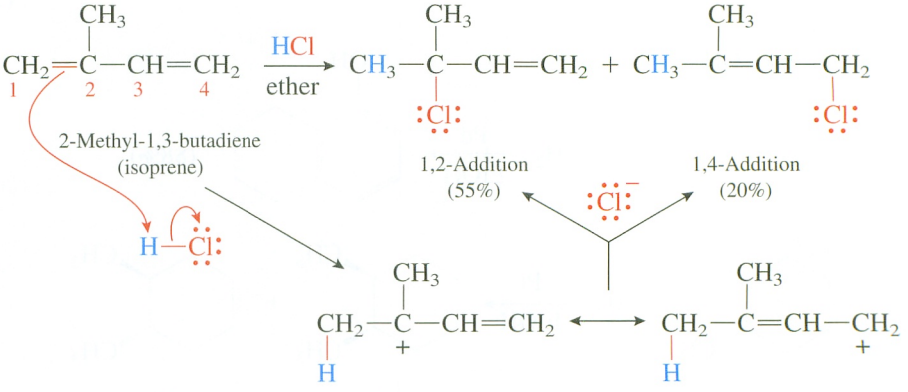
PROBLEM 11.28

Show the products of these reactions:

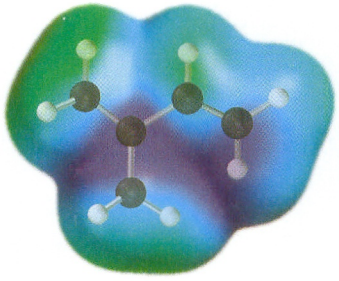


11.13 ADDITIONS TO CONJUGATED DIENES

The addition of one equivalent of a hydrogen halide to a conjugated diene results in a rapid reaction. Often, a mixture of products is formed as illustrated by the following example:



The 1,1-dimethylallyl carbocation

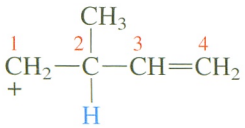


Electrostatic potential map of the 1,1-dimethylallyl carbocation

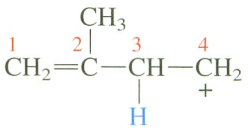
This reaction of hydrogen chloride with 2-methyl-1,3-butadiene results in the formation of 55% of the product in which the proton has added to carbon 1 and the chloride has added to carbon 2 (called 1,2-addition) and 20% of the product in which the proton has added to carbon 1 and the chloride has added to carbon 4 (called 1,4-addition). Using our knowledge of the mechanism of this reaction and what we have learned about carbocation behavior, we can easily explain these results. The reaction begins with the addition of the proton to carbon 1, producing the 1,1-dimethylallyl carbocation. (We will address why the proton adds to carbon 1 shortly.) This carbocation has two resonance structures. The positive charge is located partly on carbon 2 and partly on carbon 4. The chloride nucleophile can attack either of these carbons, resulting in the formation of the two products. In fact, given the distribution of positive charge in the carbocation, it would be very unusual if a mixture of products were not formed. The resonance struc-

ture on the left should contribute more to the resonance hybrid because it has the positive charge on a tertiary carbon, while the other structure has it on a primary carbon. In this particular case the major product results from the chloride nucleophile attacking the carbon with the larger amount of positive charge. Do not confuse this reaction with one that involves a carbocation rearrangement. This carbocation is not rearranging; it is a resonance hybrid that provides two electrophilic sites.

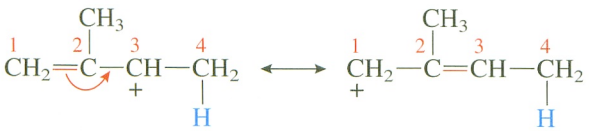
Now let's address the issue of why carbon 1 is the one that is initially protonated. According to the mechanistic rule, the electrophile—the proton—should add so as to produce the most stable carbocation. We have already seen that addition of the proton to carbon 1 produces a resonance stabilized carbocation. Addition to the other carbons produces the following carbocations:



The carbocation that results from addition of the proton to carbon 2 has the positive charge localized on a primary carbon, and there is no resonance stabilization. This carbocation is quite unstable and is not formed in the reaction.



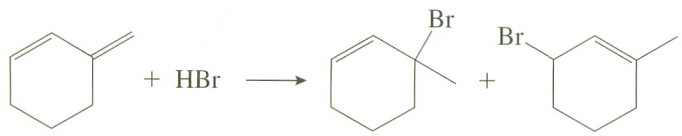
The carbocation that results from the addition of the proton to carbon 3 is similar to the previous cation in that the positive charge is localized on a primary carbon, and it has no resonance stabilization. It, also, is too unstable to be formed in the reaction.



The carbocation that results from the addition of the proton to carbon 4 has two resonance structures, so it is much more stable than the previous two carbocations. In the resonance structures for this carbocation, the positive charge is located on a secondary carbon and a primary carbon. Therefore, it is somewhat less stable than the carbocation produced by addition of the proton to carbon 1, which has the positive charge located on a tertiary carbon and a primary carbon. In accord with the mechanistic rule, the proton adds so as to produce the most stable carbocation—it adds to carbon 1.

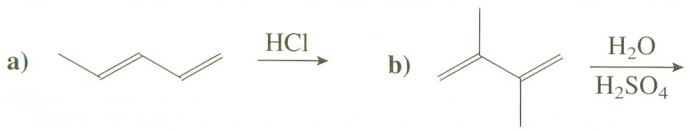
PROBLEM 11.29

Show all of the steps in the mechanism for this reaction and explain the regiochemistry of the addition:

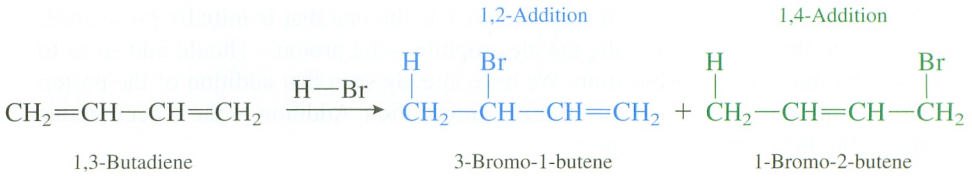


PROBLEM 11.30

Show the products of these reactions:



The composition of the product mixture formed upon electrophilic addition to conjugated dienes often changes with the temperature at which the reaction is conducted. For example, when HBr is added to 1,3-butadiene at −80°C, the major product is formed by 1,2-addition. In contrast, when the reaction is run at 45°C, the major product is the one resulting from 1,4-addition:



	3-Bromo-1-butene	1-Bromo-2-butene
At −80°C	80%	20%
At 45°C	15%	85%

Figure 11.10 shows an energy versus reaction progress diagram for this reaction. At the lower temperature, the reaction is under **kinetic control.** The rate of formation of the product determines which product is the major one. In this case, the activation energy ($\Delta G^{\ddagger}$) for the formation of the 1,2-addition product (called the kinetic product) is lower than that for formation of the 1,4-addition product, so the 1,2-addition product is formed faster, even though the 1,4-addition product is more stable.

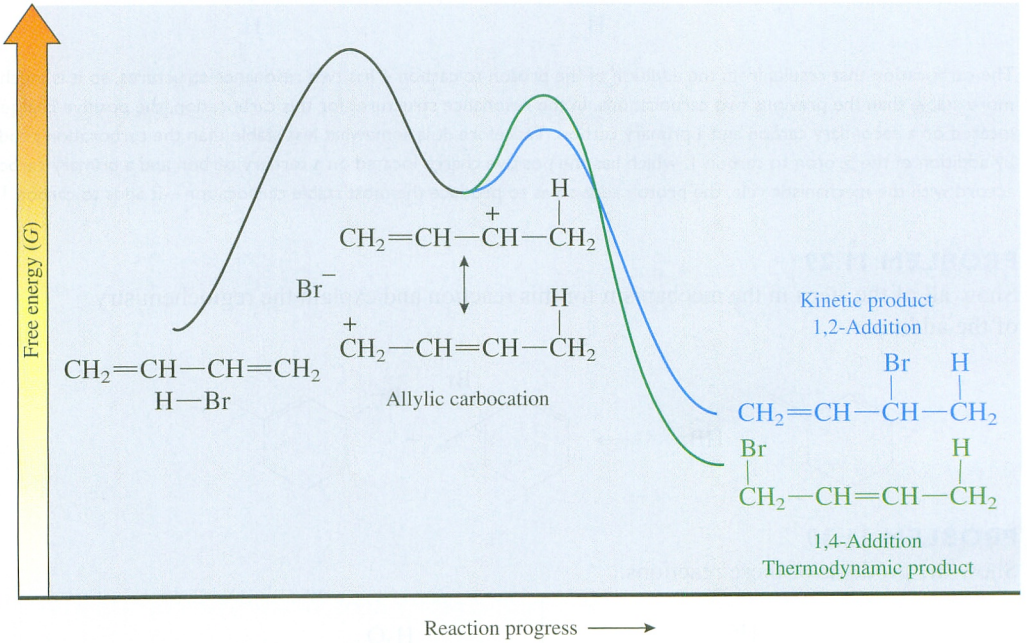


Figure 11.10

FREE ENERGY VERSUS REACTION PROGRESS DIAGRAM FOR THE ADDITION OF HBr TO 1,3-BUTADIENE.

At the higher temperature, the reaction becomes reversible and is under **thermodynamic control.** This means there is enough energy available for either product to reform the allylic carbocation by an S_N1 type ionization and then form the other product. As a result the products are in equilibrium. At equilibrium, the relative amount of the products is controlled only by the difference in energy between them (ΔG). In this case, the 1,4-addition product (called the thermodynamic product) is more stable than the 1,2-addition product, so more of it is present in the equilibrium mixture. This same equilibrium mixture of products (15% of the 1,2-addition product and 85% of the 1,4-addition product) is produced when the low-temperature reaction product mixture (80% of the 1,2-addition product and 20% of the 1,4-addition product) is heated to 45°C.

In later chapters, we will encounter several other reactions where competition occurs between the formation of the kinetic product and the thermodynamic product. However, most reactions are conducted under conditions where only one of these factors controls the product distribution. In addition, the kinetic product and the thermodynamic product are often the same, so no competition occurs in these reactions either.

Focus On

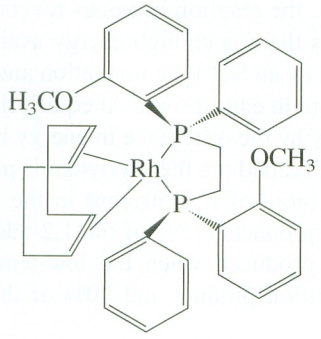
Asymmetric Hydrogenation

The Focus On box on page 433 described a hydroboration reaction that produces a single enantiomer of a chiral alcohol as the product. The chirality of one enantiomer of the boron hydride reagent is used to control the formation of a single enantiomer of the product. As discussed in that Focus On box, the drawback to this reaction is that it requires one mole of the chiral borane for each mole of chiral alcohol that is produced. The chiral reagent is rather expensive because it must be resolved or prepared from another enantiomerically pure compound. A more desirable process would use the expensive chiral reagent as a catalyst so that a much smaller amount could be employed to produce a larger amount of the chiral product.

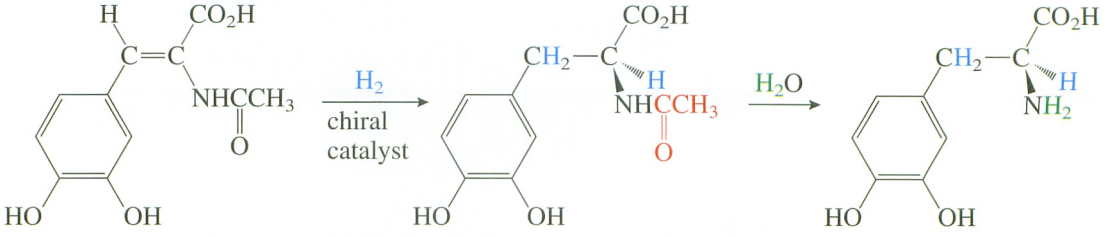
This goal has been successfully achieved in catalytic hydrogenation reactions. However, rather than use a solid metal catalyst, these reactions employ a soluble metal-containing species called a homogeneous catalyst. A homogeneous catalyst has a metal atom bonded (coordinated) to several other groups, called ligands. Because this coordinated metal atom is soluble, the reaction occurs in a single, homogeneous phase. The mechanism for the reaction is similar to that shown in Figure 11.9 for a heterogeneous catalytic hydrogenation. The metal atom still serves as a place to bond the hydrogen atoms and the alkene, helping to break bonds and stabilize intermediates so that the reaction can occur by a lower-energy pathway.

If some of the ligands bonded to the metal atom in a homogeneous catalyst are chiral, then the hydrogenation can, in theory, produce an excess of one enantiomer of the reduction product. One catalyst that has been found to be effective in such an asymmetric hydrogenation reaction is this chiral rhodium complex:

Continued

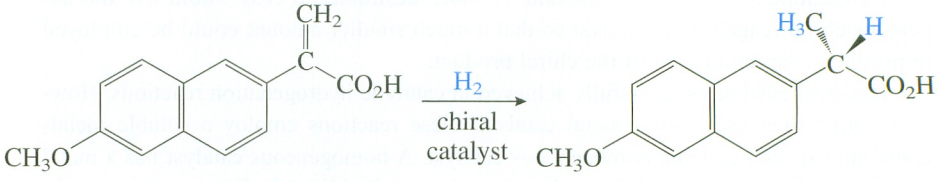


In the hydrogenation reaction the 1,5-cyclooctadiene ligand is replaced by hydrogen and the alkene and the chirality of the phosphorus ligand causes a single enantiomer of the reduced product to be formed. This process is now used industrially by Monsanto to produce L-dopa, which is used as a treatment for Parkinson's disease, from an achiral starting material:



Achiral — *S* only — (L)-3,4-Dihydroxyphenylalanine (L-dopa)

Monsanto also uses a similar process to produce a single enantiomer of the arthritis drug Naproxen, a nonsteroidal anti-inflammatory drug (NSAID). Note that this asymmetrical hydrogenation produces only the (*S*)-enantiomer of the drug in a yield of 98.5% from an achiral precursor:



Naproxen
(*S*)-Enantiomer only
(98.5%)

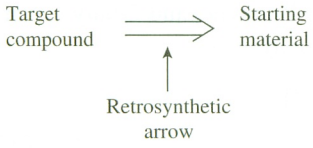
The 2001 Nobel Prize in chemistry was shared by W. S. Knowles, who developed these chiral hydrogenations at Monsanto; R. Noyori, who also worked in the area of chiral hydrogenations; and K. B. Sharpless, who developed methods for chiral epoxidation reactions.

11.14 SYNTHESIS

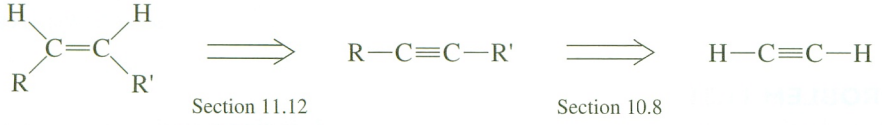
As described in Section 10.15, a common task confronted by an organic chemist is the synthesis of a desired compound that is not available from commercial sources. Now that we have the addition reactions of this chapter available, let's practice designing some more complicated syntheses.

Recall that the best way to approach planning a synthesis is to use retrosynthetic analysis, that is, to work backward from the desired compound, the target, to simpler compounds, until an available compound is reached. *A special type of reaction arrow, called the* **retrosynthetic arrow,** *is useful in such a synthetic analysis. As shown in the following example, the retrosynthetic arrow points from the target to the reactant.* Usually, the reagents that cause the transformation are not specified, although it is necessary to have some method in mind that will accomplish the transformation. After retrosynthetic analysis has led to a reasonable starting material, the synthesis is written in the forward direction and all the necessary reagents are included.

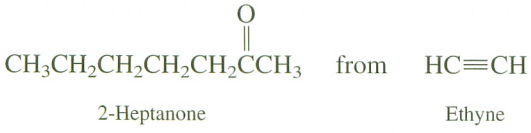
Important Convention



Reactions that form carbon–carbon bonds are extremely important in synthesis because they enable larger compounds, containing more carbons, to be constructed from smaller compounds. This requires the reaction of a carbon nucleophile with a carbon electrophile. The most important carbon nucleophiles that we have encountered so far are cyanide ion and acetylide anions (see Section 10.8). If we remember that acetylide anions can be reduced to *cis*-alkenes (see Section 11.12), then all of the addition products of this chapter are accessible from simple alkynes.

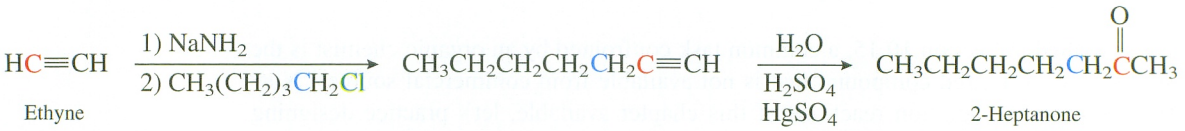


Let's try a synthesis. Suppose we are asked to synthesize 2-heptanone from ethyne.



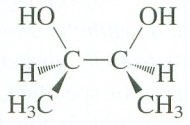
First we note that it is necessary to form a carbon–carbon bond because the starting material has only two carbons and the target has seven. Because the starting material is an alkyne, we can probably use an acetylide anion as the nucleophile to form the carbon–carbon bond (see Section 10.8). How can a ketone functional group be introduced? Section 11.6 described the hydration of an alkyne to produce a ketone. Our retrosynthetic analysis then becomes:

Written in the forward direction, the synthesis is as follows:



Ethyne 2-Heptanone

Let's try another example. This time our assignment is to prepare *meso*-2,3-butanediol from propyne:

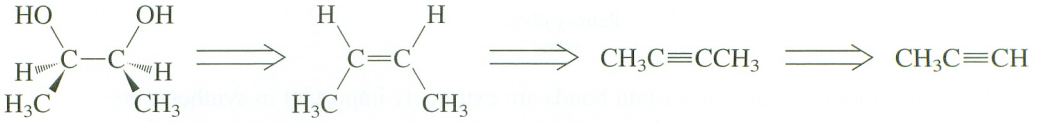


meso-2,3-Butanediol

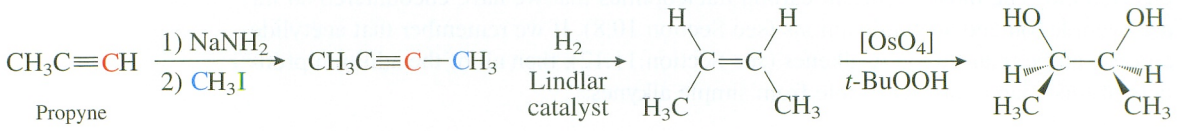
from $CH_3C{\equiv}C{-}H$

Propyne

The diol can be prepared from syn hydroxylation of (*Z*)-2-butene. The *cis*-alkene can be prepared by hydrogenation of 2-butyne, and 2-butyne can be prepared by alkylation of propyne. The retrosynthetic analysis is:



Written in the forward direction, the synthesis is as follows:



Propyne *meso*-2,3-Butanediol

PROBLEM 11.31

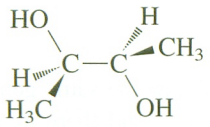
Show syntheses of these compounds from the indicated starting materials. Your syntheses may produce both enantiomers of any target that is chiral.

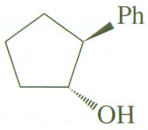
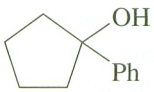
a) $CH_3CH_2CH_2CH_2CH_2OCH_3$ from $CH_3CH_2CH_2CH{=}CH_2$

b) $CH_3\underset{\displaystyle CH_3}{\underset{|}{C}}HCH_2CH_2\overset{\displaystyle O}{\overset{\|}{C}}CH_3$ from $HC{\equiv}CH$

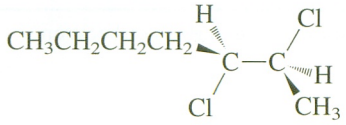
c) $PhCH_2CH_2CH_2\overset{\displaystyle O}{\overset{\|}{C}}H$ from $HC{\equiv}CH$

d) $CH_3CH_2\overset{\displaystyle O}{\overset{\|}{C}}CH_2CH_2CH_3$ from $HC{\equiv}CH$

e)  from $CH_3C{\equiv}CCH_3$

f)  from 

g) $CH_3CH_2CH_2\underset{\displaystyle CN}{\underset{|}{C}}HCH_3$ from $CH_3CH_2CH_2CH{=}CH_2$

h)  from $CH_3CH_2CH{=}CH_2$

Review of Mastery Goals

After completing this chapter, you should be able to:

- Show the products, including regiochemistry and stereochemistry, resulting from the addition to alkenes of all of the reagents listed in this chapter. (Problems 11.32, 11.33, 11.34, 11.35, 11.43, 11.55, 11.56, 11.57, 11.58, 11.59, 11.60, 11.61, and 11.62)
- Show the products, including regiochemistry and stereochemistry, resulting from the addition to alkynes of all of the reagents listed in this chapter. These reagents include HX, X_2, $Hg^{2+}/H^+/H_2O$, disiamylborane, and H_2. (Problems 11.32 and 11.33)
- Show the mechanisms for any of these reactions. (Problems 11.36, 11.39, 11.41, 11.42, and 11.44)
- Show rearranged products when they are likely to occur. (Problems 11.32f and 11.33c)
- Predict how the rate of addition varies with the structure of the alkene. (Problem 11.40)
- Predict the products from additions to conjugated dienes. (Problem 11.33o)
- Use these reactions in synthesis. (Problems 11.37 and 11.38)

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Click *Mastery Goal Quiz* to test how well you have met these goals.

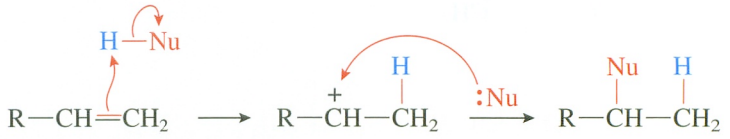
Visual Summary of Key Reactions

This chapter presented many reactions. Although most of them follow the same general mechanism in which an electrophile adds to the carbon–carbon double bond, there are several variations on this mechanism. In addition, the regiochemistry and/or the stereochemistry of the reaction may be important. Complications, such as carbocation rearrangements, may occur. You will have an easier time remembering all these details if you organize the reactions according to the three variations of the mechanism that they follow.

Table 11.2 summarizes the reactions in which a proton electrophile adds to produce a carbocation intermediate (hydrohalogenation and hydration). These reactions follow Markovnikov's rule and tend to give mixtures of stereoisomers when possible. They are very prone to carbocation rearrangements.

Table 11.2 Addition Reactions Following a Carbocation Mechanism

These reactions proceed by initial addition of a proton to the alkene to give a carbocation intermediate. The nucleophile adds in the second step.



Reagent	Product	Comments
H—Cl (HF, HBr, HI) (Section 11.2)	Cl H R—CH—CH2	All of these reactions proceed with Markovnikov orientation and random stereochemistry. Watch for carbocation rearrangements.
H_3O^+ (Section 11.3)	OH H R—CH—CH2	

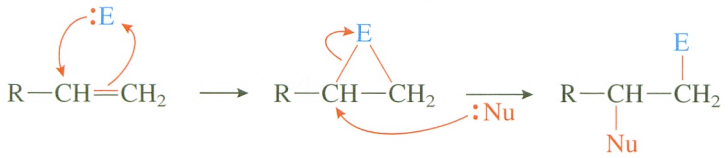
Table 11.3 summarizes the reactions that proceed through a three-membered cyclic intermediate. In each of these reactions the electrophile has an unshared pair of electrons, so it can also act as a nucleophile. The electrophile adds to form the three-membered ring in a syn manner. If the electrophilic atom is uncharged, then the reaction stops at this cyclic stage (carbenes, epoxidation). If the electrophile has a positive charge in the ring, then a nucleophile adds in a second step (halogenation, halohydrin formation, oxymercuration, mercury-catalyzed hydration of alkynes). The regiochemistry of the addition is such that the nucleophile attaches to the carbon that would be more stable as a carbocation and the addition occurs with anti stereochemistry.

Table 11.4 summarizes the reactions in which the electrophile and the nucleophile are linked in the same molecule (hydroboration, hydroxylation, ozonolysis). These additions occur in a concerted manner. The regiochemistry of the addition is such that the nucleophile attaches to the carbon that would be more stable as a carbocation and the addition occurs with syn stereochemistry.

Table 11.5 summarizes the catalytic hydrogenation reactions that can be used to add hydrogens to double or triple bonds, converting alkenes and alkynes to alkanes or alkynes to *cis*-alkenes.

Table 11.3 Addition Reactions Proceeding through a Three-Membered Cyclic Intermediate

When the electrophile also has an unshared pair of electrons, addition initially produces a three-membered ring. If the ring is uncharged, the reaction stops here. If the ring has a positive charge, a nucleophile attacks and opens the ring.



Syn addition

Anti addition

Stops here if neutral; adds Nu if E has +.

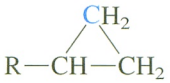
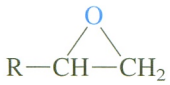
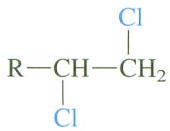
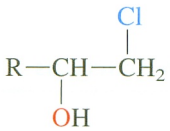
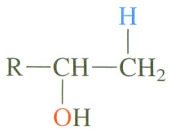
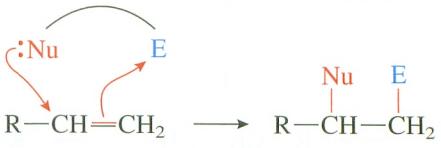
Reagent	Product	Comments
CH_2N_2 (CHX_3/OH^-) (CH_2I_2, Zn/Cu) (Section 11.8)		Carbenes add to give cyclopropane derivatives. These are syn additions. The Simmons-Smith reaction generates a carbenoid that reacts like methylene.
$R'CO_3H$ (Section 11.9)		Percarboxylic acids add to alkenes to give epoxides in a syn addition.
Cl_2 (Br_2)		Chlorine and bromine add with anti stereochemistry.
Cl_2/H_2O (Br_2/H_2O) (Section 11.4)		In water as solvent, Cl_2 and Br_2 add to give halohydrins, with the OH on the more substituted carbon and anti stereochemistry.
1) $Hg(O_2CCH_3)_2$, H_2O 2) $NaBH_4$, NaOH (Section 11.6)		The oxymercuration reaction is a method for the Markovnikov addition of water without rearrangement.
Hg^{2+}, H_2O, H_2SO_4 (Section 11.6)		The initial product, an enol, tautomerizes to a ketone.

Table 11.4 Addition Reactions Where the Nucleophile and Electrophile Are Linked

When the electrophile and nucleophile are part of the same molecule, concerted additions occur with syn stereochemistry.



Syn addition

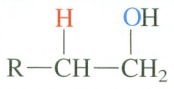
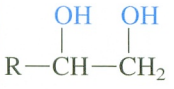
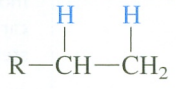
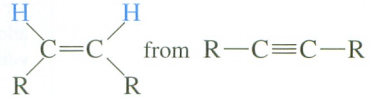
Reagent	Product	Comments
1) BH_3, THF 2) H_2O_2, NaOH (Section 11.7)		The hydroboration reaction results in anti-Markovnikov addition of water with syn stereochemistry.
1) Disiamylborane 2) H_2O_2, NaOH (Section 11.7)		The reaction of 1-alkynes with the hindered borane produces aldehydes.
OsO_4, *t*-BuOOH or $KMnO_4$, H_2O, NaOH (Section 11.10)		Osmium tetroxide and permanganate result in the syn addition of hydroxy groups to the alkene.
1) O_3 2) $(CH_3)_2S$ (Section 11.11)		Ozone can be used to cleave the alkene to two carbonyl compounds.

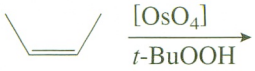
Table 11.5 Catalytic Hydrogenation Reactions

Reagent	Product	Comments
H_2, cat. (Ni, Pd, Pt) (Section 11.12)		Catalytic hydrogenation results in the addition of hydrogen to the alkene.
H_2 Lindlar catalyst (Section 11.12)		Addition of hydrogen to an alkyne using Lindlar catalyst produces a *cis*-alkene.

Integrated Practice Problem

Show the products of these reactions:

a)  + HCl ⟶ b)  + Br_2 ⟶

c) 

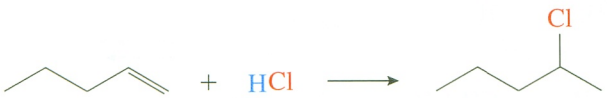
Strategy

As usual, the key is to identify the electrophile and the nucleophile. Add these to the pi bond with the nucleophile bonded to the carbon that would be more stable as a carbocation. Identification of the mechanism type that is being followed will help you remember the details of the reaction, such as the stereochemistry.

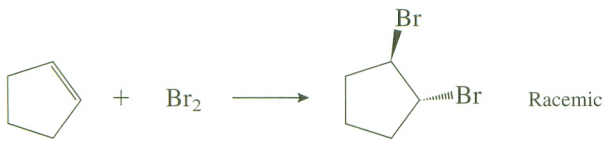
- If the electrophile is H^+, then the reaction is one from Table 11.2 and proceeds through a carbocation intermediate. Watch for rearrangements.
- If the electrophile has an unshared pair of electrons, the reaction is one from Table 11.3 and proceeds through a three-membered cyclic intermediate, which is formed by syn addition. If the cyclic intermediate is neutral, the reaction stops here. If the intermediate is charged, the nucleophile adds with inversion (borderline S_N2 mechanism), resulting in overall anti addition.
- If the electrophile and nucleophile are part of the same molecule, the reaction is one from Table 11.4 and the addition is syn.

Solutions

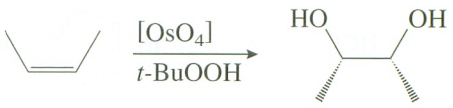
a) The electrophile is H^+ and the nucleophile is Cl^-. The reaction is one from Table 11.2. It proceeds through a carbocation, but rearrangement will not occur because a more stable carbocation cannot be readily generated. The nucleophile is bonded to carbon 2 because this carbon (secondary) would be more stable as a carbocation than carbon 1 (primary).



b) The electrophile is Br^+ and the nucleophile is Br^-. Because the electrophile has an unshared electron pair, the reaction is one from Table 11.3. The cyclic bromonium ion is charged, so the bromide nucleophile adds in the second step resulting in overall anti addition.



c) Both the electrophile and the nucleophile are oxygens bonded to osmium. The reaction is one from Table 11.4. The reaction results in syn addition of two OH groups to the alkene.



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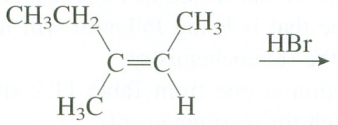
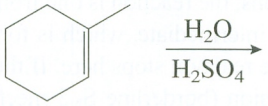
Additional Problems

11.32 Show the products of these reactions:

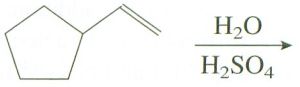
a) 

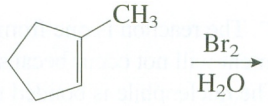
b) 

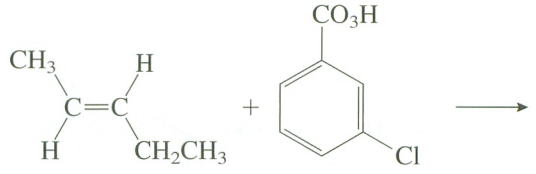
c) 

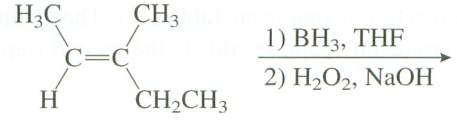
d) 

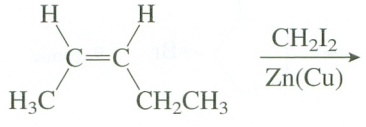
e) $CH_3CH_2CH_2C{\equiv}CH$ $\xrightarrow[H_2SO_4,\ HgSO_4]{H_2O}$

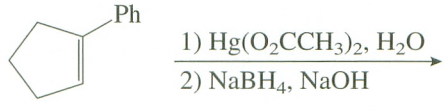
f) 

g) 

h) 

i) 

j) 

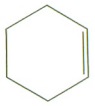
k) 

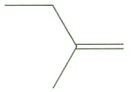
l) $PhC{\equiv}CH \xrightarrow{2\ HCl}$

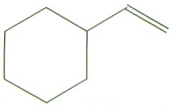
m) $CH_3CH_2C{\equiv}CCH_2CH_3 \xrightarrow[\text{Lindlar catalyst}]{1\ H_2} \xrightarrow[t\text{-BuOOH}]{[OsO_4]}$

n) $PhCH_2C{\equiv}CH \xrightarrow[2)\ H_2O_2,\ NaOH]{1)\ \text{disiamylborane}}$

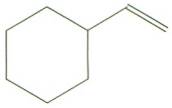
11.33 Show the products of these reactions.

a)  $\xrightarrow[KOH]{CHBr_3}$

b)  $\xrightarrow[H_2SO_4]{H_2O}$

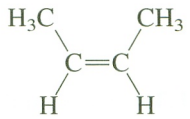
c)  $\xrightarrow{HCl}$

d) $PhC{\equiv}CPh \xrightarrow[H_2SO_4\ HgSO_4]{H_2O}$

e)  $\xrightarrow[2)\ NaBH_4,\ NaOH]{1)\ Hg(O_2CCH_3)_2,\ H_2O}$

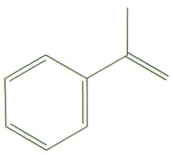
f) $CH_3CHCH_2CH{=}CH_2$ (CH_3 on the second carbon) $\xrightarrow[2)\ H_2O_2,\ NaOH]{1)\ BH_3,\ THF}$

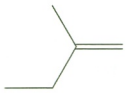
g) $CH_3CH_2CH_2C{\equiv}CH \xrightarrow[2)\ H_2O_2,\ NaOH]{1)\ (CH_3CHCH_2)_2BH}$

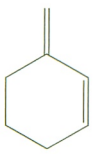
h)  $\xrightarrow{CH_3CO_3H}$

i)  $\xrightarrow[CH_2Cl_2]{Br_2}$

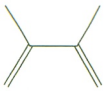
j)  $\xrightarrow[t\text{-BuOOH}]{[OsO_4]}$

k)  $\xrightarrow[Pt]{H_2}$

l)  $\xrightarrow[H_2O]{Br_2}$

m)  $\xrightarrow[2)\ (CH_3)_2S]{1)\ O_3}$

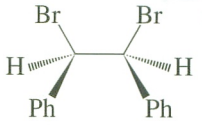
n) $CH_3C{\equiv}CCH_3 \xrightarrow[CCl_4]{1\ Br_2}$

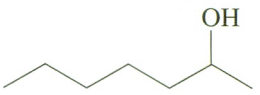
o)  $\xrightarrow{HBr}$

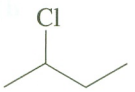
11.34 Show the products of the reactions of 1-propylcyclopentene with these reagents:

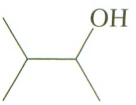
a) Br_2, CCl_4
b) Br_2, H_2O
c) 1) BH_3, THF; 2) H_2O_2, NaOH
d) HBr
e) H_2O, H_2SO_4
f) $[OsO_4]$, *t*-BuOOH
g) 1) O_3; 2) $(CH_3)_2S$

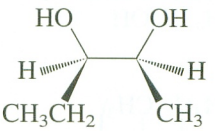
11.35 Show the alkenes that would give these products. More than one answer may be possible in some cases.

a) $\xrightarrow[CCl_4]{Br_2}$ 

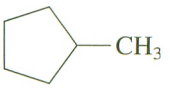
b) $\xrightarrow[2)\ NaBH_4,\ NaOH]{1)\ Hg(O_2CCH_3)_2,\ H_2O}$ 

c) $\xrightarrow{HCl}$ 

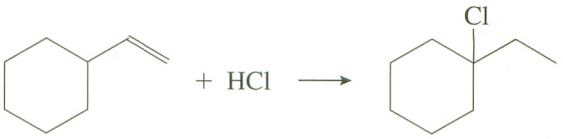
d) $\xrightarrow[2)\ H_2O_2,\ NaOH]{1)\ BH_3,\ THF}$ 

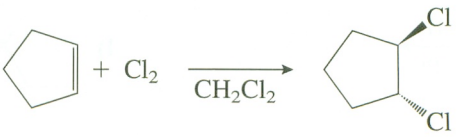
e) $\xrightarrow[t\text{-BuOOH}]{OsO_4}$ 

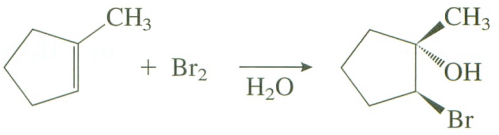
Racemic

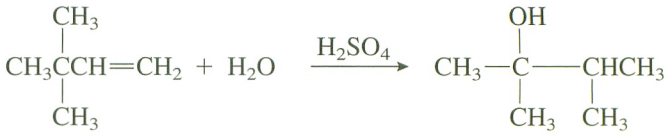
f) $\xrightarrow[Pd]{H_2}$ 

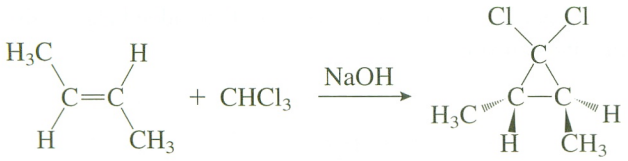
11.36 Show all the steps in the mechanisms for these reactions. Include stereochemistry where it is important.

a) 

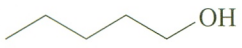
b) 

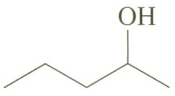
c) 

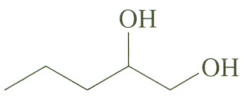
d) 

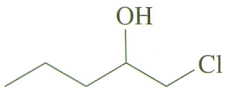
e) 

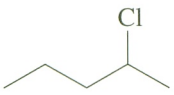
11.37 Show reactions that could be used to convert 1-pentene to these compounds. More than one step may be necessary.

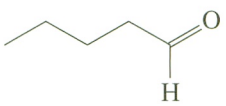
a) 

b) 

c) 

d) 

e) 

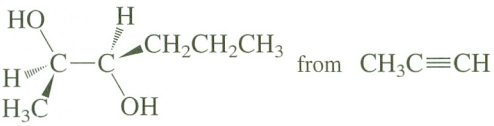
f) 

g) 

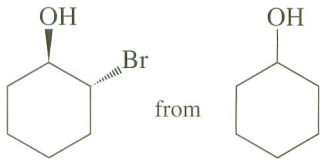
h) 

11.38 Show syntheses of these compounds from the indicated starting materials. More than one step may be necessary. Your syntheses may produce both enantiomers of any target that is chiral.

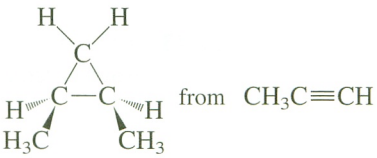
a) 

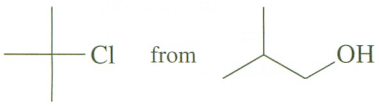
b) 

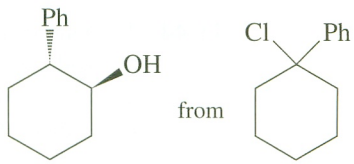
c) 

d) 

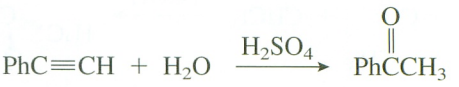
e) 

f) 

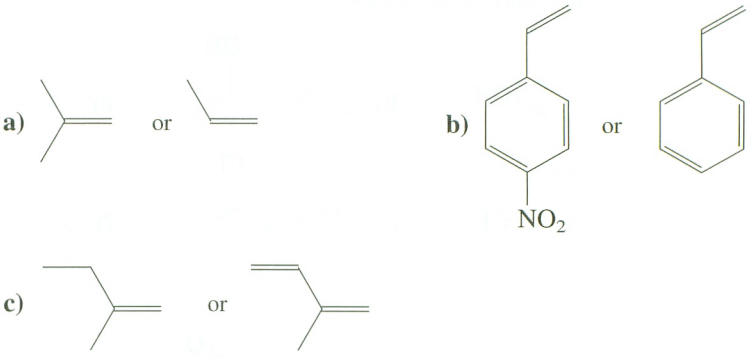
g) 

h) 

11.39 This alkyne hydration reaction can occur without added Hg^{2+}. Show all the steps in the mechanism.



11.40 Explain which compound has a faster rate of reaction with HCl:



11.41 The addition of Cl_2 to (*E*)-2-pentene produces a racemic mixture of (2*R*,3*S*)-2,3-dichloropentane and its enantiomer, (2*S*,3*R*)-2,3-dichloropentane.

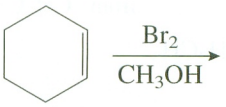
a) Show the structures of the two chloronium ions that are formed in this reaction. What is the relationship between them?

b) What is the relationship of the products that are formed by attack of the chloride nucleophile at each carbon of the two chloronium ions?

c) Explain why the percentages of nucleophile attack at the two carbons of one chloronium ion are not necessarily identical.

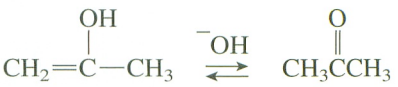
d) Explain why the product that is formed must be racemic.

11.42 Show the steps in the mechanism and predict the product that would be formed in this reaction:



11.43 The oxymercuration reaction can be run in methanol as the solvent rather than water. Predict the product of this reaction:

11.44 The tautomerization of an enol to a ketone is catalyzed by either acid or base. In the acid-catalyzed mechanism, H^+ is added in the first step (see Figure 11.6). In the base-catalyzed mechanism, H^+ is removed in the first step. Show the steps in the mechanism for the base-catalyzed tautomerization.



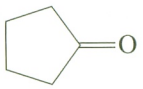
11.45 An unknown compound has the formula C_6H_{10}.

a) What is the DU for this compound?

b) When a solution of Br_2 in CCl_4 is added to the unknown, the bromine color disappears. What information does this provide about the structure of the unknown?

c) The unknown reacts with excess H_2 in the presence of Pt to give C_6H_{12}. What information does this provide about the structure of the unknown?

d) This ketone is one of the products isolated from the ozonolysis of the unknown. What is the structure of the unknown?



11.46 An unknown compound has the formula C_7H_{12}.

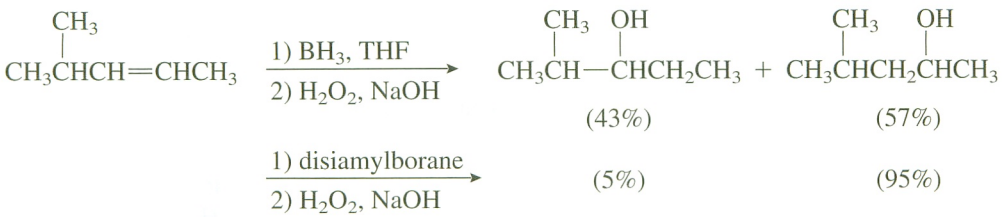
a) What is the DU for this compound?

b) The unknown reacts with H_2 in the presence of Pd to give C_7H_{16}. What information does this provide about the structure of the unknown?

c) The unknown reacts with H_2 in the presence of Lindlar catalyst to give C_7H_{14}. What information does this provide about the structure of the unknown?

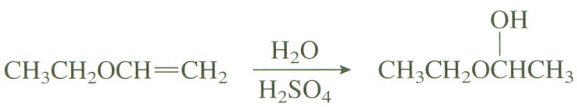
d) The product from part c, C_7H_{14}, gives these two aldehydes upon ozonolysis. Show the structure of the original unknown.

11.47 Explain the difference in the percentages of the products in these two hydroboration reactions:



11.48 Explain why this reaction occurs with anti-Markovnikov regiochemistry:

11.49 Explain why the hydration of this alkene occurs 10^{15} times faster than the hydration of ethene:



11.50 The addition of HCl to alkynes proceeds through a vinyl cation intermediate. Explain which of the two possible vinyl cations that could be formed from the addition of HCl to propyne is more stable.

A vinyl cation

11.51 Suggest a mechanism for this reaction:

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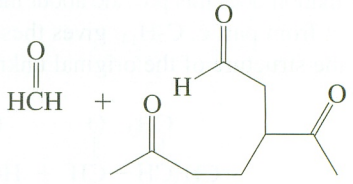
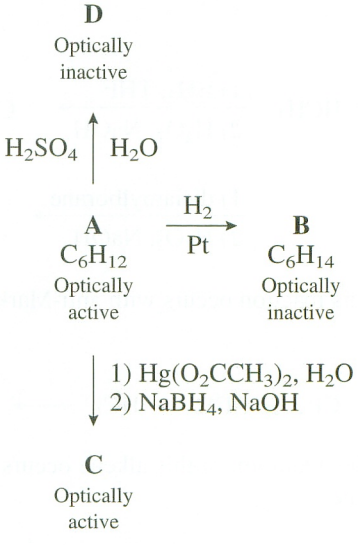
11.52 Limonene, a major component of lemon oil, has the formula $C_{10}H_{16}$.

a) On reaction with excess H_2 in the presence of Pt, limonene produces $C_{10}H_{20}$. What information does this provide about the structure of limonene?

b) On ozonolysis, limonene produces these compounds. Suggest possible structures for limonene.



11.53 Show the structures of **A, B, C,** and **D** in the following reaction scheme:



11.54 In Figure 11.3, suppose Br_2 adds to the alkene from the bottom, rather than from the top as shown. Analyze the stereochemistry of the reaction in this case and explain which products are formed.

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11.55 Explain which of the three products shown is formed when 1-butene reacts with HCl.

11.56 Explain which of the four products shown is formed when *cis*-2-pentene reacts with Cl_2.

11.57 Explain which of the four products shown is formed when cyclopentene reacts with Cl_2 and water.

11.58 Explain which of the five products shown is formed when 1-ethylcyclopentene reacts with BH_3 in THF, followed by treatment with NaOH and H_2O_2.

11.59 Explain which of the three products shown is formed when *trans*-2-butene reacts with CH_2I_2 and Zn(Cu).

11.60 Explain which of the three products shown is formed when *cis*-2-butene reacts with OsO_4 and *t*-BuOOH.

11.61 The hydroboration–oxidation of α-pinene gives the product shown. Carefully explain the regiochemistry and the stereochemistry of this reaction.

11.62 The catalytic hydrogenation of the alkene shown gives the product shown. The hydrogens that added to the double bond are blue in the product. Explain the stereochemistry of this reaction.